Ana Beatriz Francioso de Oliveira[1], Olivia Meira Dias[2], Marcos Moreira Mello[3], Sebastião Araújo[4], Desanka Dragosavac[5], Anamarli Nucci[6], Antônio Luis Eiras Falcão[7]

Factors associated with increased mortality and prolonged length of stay in an adult intensive care unit

Fatores associados à maior mortalidade e tempo de internação prolongado em uma unidade de terapia intensiva de adultos

1. Physiotherapist, Post-graduation Student of the Department of Surgery of the Faculdade de Ciências Médicas (FCM) of Universidade Estadual de Campinas – UNICAMP – Campinas (SP), Brazil.
2. Pneumology Resident Physician of the Universidade de São Paulo – USP – São Paulo (SP), Brazil.
3. Physiotherapist, Post- graduate Student of the Department of Surgery of the Faculdade de Ciências Médicas (FCM) of Universidade Estadual de Campinas – UNICAMP – Campinas (SP), Brazil.
4. PhD, Assistant Professor for the Department of Surgery of the Faculdade de Ciências Médicas (FCM) of Universidade Estadual de Campinas – UNICAMP – Campinas (SP), Brazil.
5. PhD, Assistant Professor for the Department of Surgery of the Faculdade de Ciências Médicas (FCM) of Universidade Estadual de Campinas – UNICAMP – Campinas (SP), Brazil.
6. Full Professor for the Department of Neurology of the Faculdade de Ciências Médicas (FCM) of Universidade Estadual de Campinas – UNICAMP – Campinas (SP), Brazil.
7. PhD, Assistant Professor for the Department of Surgery of Faculdade de Ciências Médicas (FCM) of Universidade Estadual de Campinas – UNICAMP – Campinas (SP), Brazil; Physician of the Adult ICU of the Hospital das Clínicas of Universidade Estadual de Campinas – UNICAMP – Campinas (SP), Brazil.

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Author for correspondence:
Ana Beatriz Francioso de Oliveira
Centro de Atenção Integral á Saúde da Mulher (CAISM – UNICAMP)
Serviço de Fisioterapia
Rua Alexandre Flemming – Cidade Universitária
Zip Code: 13083-881 – Campinas (SP), Brazil.
Phone: +55 19 35219428 / 35219483
E-mail: anabiafisio@yahoo.com.br

ABSTRACT

Objective: The intensive care unit is synonymous of high severity, and its mortality rates are between 5.4 and 33%. With the development of new technologies, a patient can be maintained for long time in the unit, causing high costs, psychological and moral for all involved. This study aimed to evaluate the risk factors for mortality and prolonged length of stay in an adult intensive care unit.

Methods: This study included all patients consecutively admitted to the adult medical/surgical intensive care unit of the Hospital das Clínicas of Universidade Estadual de Campinas in a six-month period. Data such as gender, age, diagnosis, medical history, APACHE II score, days of invasive mechanical ventilation, orotracheal reintubation, tracheostomy, hospitalization days in the intensive care unit and outcome (either discharge or death) were collected.

Results: Four hundred and one patients were included in this study of which 59.6% were men and 40.4% women with mean age of 18.0 ±53.8 years, the mean intensive care unit stay was 8.2±10.8 days and the mortality rate was 13.5%. APACHE II>11, tracheostomy and reintubation were significantly associated ($p<0.0001$) with mortality and prolonged intensive care unit stay.

Conclusion: The risk factors for increased mortality and prolonged intensive care unit stay were: APACHE>11, orotracheal reintubation and tracheostomy.

Keywords: Intensive care unit; Mortality; Length of stay; Risk factors

INTRODUCTION

The intensive care unit (ICU) is specially dedicated to patients who are able to be recovered from severe and/or high risk diseases and require continuous medical care, multi-professional health care team, and other specialized human resources, in addition to special devices.[1] Intensive care unit stands for urgency and its mortality rates range between 5.4 and 33%.[2-5]

According to the 2nd Brazilian ICU Census, the Brazilian ICU average stay is between one and six days[6] and in a systematic literature review, Williams *et al.*[3] reported an international average of 5.3 ± 2.6 days. However, due to continuous technological development, severely ill patients are currently kept in these units for long periods of time, even when death is not avoidable, entailing heavy financial, moral and psychological burdens.[7]

This study was aimed to identify the factors associated with increased mortality and prolonged length of stay in an adult ICU.

METHODS

A prospective study was conducted on the clinical/surgical adult ICU of the Hospital de Clínicas of Universidade Estadual de Campinas (HC/UNICAMP) which included all patients consecutively admitted to the unit in a six-month period. Patients with missing data, transferred to other hospitals before discharge from the ICU and with unfeasible follow-up due to lost data or incorrect records were excluded.

The patients were characterized by gender, age, diagnosis, medical history (including chronic systemic arterial hypertension [SAH], diabetes mellitus [DM], chronic obstructive pulmonary disease [COPD], smoking status, alcoholism, liver failure, renal failure and cancer) obtained from the patients' medical chart within the first 24 hours of admission. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score was used to determine the primary disease's severity. All clinical and laboratory data for the score calculation were part of the patient's routine care. Other daily collected information were: invasive mechanical ventilation (IMV) days, orotracheal reintubation (ReOTI), tracheostomy, ICU length of stay and ICU outcome (discharge/death).

The IMV time was considered as the period elapsed from orotracheal intubation (OTI) to successful extubation provided that the patient remained at least 24 hours without mechanical ventilation. Patients not requiring OTI or with less than 24 hours mechanical ventilation were included in the IMV < 24 hours group. In this study, the ICU length of stay was considered prolonged when lasting more than seven days.

The data were described by the mean and standard deviation calculations. Prevalence was calculated by the Chi-square test or the Fisher's exact test. The risk of death was estimated by odds ratio (crude) calculation and its respective 95% confidence interval. The risk-of-death factors were analyzed by multivariate logistic regression, using stepwise selection criteria. For every statistics a 5% level of significance was considered. The analyses were conducted with the 9.1 version SAS software.

RESULTS

During the 6-month period, 422 patients were admitted to the adult ICU of the HC-UNICAMP. Twenty one patients were excluded: one due to transference to another service, one for incorrect data, and nineteen for incomplete medical chart data. Four hundred and one patients were included, of which 239 (56.9%) were males and 162 (40.4%) females. The mean age was 53.8 ± 18.0 years. Ninety patients (22.4%) were under 40 years of age, 155 (38.7%) between 40 and 60 years, and 156 (38.9%) over 60 years of age.

The mean APACHE II score was 12.0 ± 5.6, median 11; 206 (51.4%) patients had APACHE II score below 11, whereas among 195 (48.6%) this score was above 11 (Tables 1 and 2). One hundred and twenty-five (31.2%) patients stayed longer than 7 days in the ICU, with a mean length of ICU stay between 8.2± 10.8 days, median 4, range 1 to 109. One hundred and ninety-one (47.6%) patients were admitted extubated or remained less than 24 hours under IMV, 210 (52.4%) remained mechanically ventilated ≥ 24 hours and 75 (35.7%) were ≥ 7 days under invasive mechanical ventilation. The mean IMV days was 9.3 ± 14.3, median 3, range 1 to 98. Among the 210 pa-

Table 1 – Overall sample characteristics

Characteristics	N = 401	%
Gender		
Male	239	59.6
Female	162	40.4
Age (years)		
< 40	90	22.4
40-60	155	38.7
> 60	156	38.9
APACHE II		
Up to 11	206	51.4
> 11	195	48.6
Invasive mechanical ventilation		
< 24 h	191	47.6
≥ 24 h	210	52.4
ICU length of stay		
< 7 days	276	68.8
≥ 7 days	125	31.2

APACHE II - Acute Physiology and Chronic Health Evaluation; ICU - intensive care unit.

Table 2 – Overall sample characteristics

Variables	N	Result
Age (years)	401	53.8 ± 18.0
APACHE II	401	12.0 ± 5.6
ICU length of stay (days)	401	8.2 ± 10.8
IMV time (days)	210	9.3 ± 14.3
Tracheostomy time (days)	55	9.4 ± 4.9

APACHE II - Acute Physiology and Chronic Health Evaluation; ICU – intensive care unit; IMV – invasive mechanical ventilation. Data expressed as mean ± standard deviation.

Table 3 – Above 24 hours invasive mechanical ventilation sample characteristics

Characteristics	N = 210	%
Invasive mechanical ventilation days		
< 7 days	135	64.3
≥ 7 days	75	35.7
Tracheostomy		
No	155	73.8
Yes	55	26.2
Reintubation		
No	178	84.8
Yes	32	15.2

Table 4 – Causes of reintubation

Causes	N = 32	%
Upper airways obstruction	5	15.6
Hypoxemia	6	18.8
Increased respiratory load	13	40.6
Reduced consciousness level	5	15.6
Reoperation	1	3.1
Others	2	6.3

tients, fifty-five (26.2%) underwent tracheostomy, and the mean IMV days before tracheostomy was 9.4 ± 4.9. Thirty-two (15.2%) patients were reintubated (Tables 1, 2 and 3). The main ReOTI causes were: post-extubation upper airways obstruction (15.6%); hypoxemia (SaO_2 < 90%, or PaO_2 < 60 mmHg with FiO_2 > 50%) (18.8%); increased respiratory load (intercostal, diaphragm or furcula sampling, use of accessory muscles or paradoxical breathing), reduced consciousness level (15.6%), reoperation (3.1%) and others (6.3%) (Table 4).

The entire ICU population mortality rate was 13.46%. No significant gender influence on mortality was identified. However, in the multivariate analysis patients between 40 and 60 years old had increased the risk of death (OR 3.86; 95%CI 1.39-10.70).

APACHE II score > 11 (OR 5.01; 95%CI 2.50-10.05; *P*<0.0001), ReOTI (OR 8.71; 95%CI 4.03-18.81; *P*<0.0001), ≥ 7 days IMV (OR 3.82; 95%CI 1.99-7.36; *P*<0.0001) and tracheostomy (OR 5.09; 95%IC 2.66-9.77; *P*<0.0001) were also pointed out as mortality risk factors (Table 5).

Regarding prolonged ICU stay no significant dif-

Table 5 – Analysis of risk factors associated with mortality

Variable	Discharge N = 347	Death N = 54			Univariate OR	Multivariate OR
	N	N	%	p value	OR (95%CI)	OR (95%CI)
Gender				0.21		NS
Male	211	28	11.7		1.00	
Female	136	26	16.0		1.44 (0.81 - 2.56)	
Age				0.80		
< 40	79	11	12.2		1.00	1.00
40 to 60	132	23	14.8		1.25 (0.58 - 2.70)	3.86 (1.39 - 10.70)
> 60	136	20	12.8		1.06 (0.48 -2.32)	1.81 (0.65 - 5.04)
APACHE II				< 0.0001		NS
Up to 11	195	11	5.3		1.00	
> 11	152	43	22.1		5.01 (2.50 - 10.05)	
ReOTI				< 0.0001		
No	331	38	10.3		1.00	1.00
Yes	16	16	50.0		8.71 (4.03 - 18.81)	4.67 (1.74 - 12.56)
IMV time (days)				< 0.0001		NS
< 7 days	114	21	15.6		1.00	
≥ 7 days	44	31	41.3		3.82 (1.99 - 7.36)	
Tracheostomy				< 0.0001		NS
No	312	35	10.1		1.00	
Yes	35	20	36.4		5.09 (2.66 - 9.77)	

Chi-square test; * Fisher's exact test; stepwise logistic regression; NS – non-significant; IMV – invasive mechanical ventilation; ReOTI – orotracheal reintubation; DInterUTI – ICU length of stay (days); DVMI – days in invasive mechanical ventilation; APACHE II - Acute Physiology and Chronic Health Evaluation.

Table 6 – Analysis of risk factors for prolonged intensive care unit stay

Variable	< 7 days N = 276	≥ 7 days N = 125				
	N	N	%	p value	Univariate OR OR (95%CI)	Multivariate OR OR (95%CI)
Gender				0.9123		NS
Male	165	74	31.0		1.00	
Female	111	51	31.5		1.02 (0.67 - 1.58)	
Age (years)				0.0109		NS
< 40	53	37	41.1		1.00	
40 to 60	119	36	23.2		0.43 (0.25 - 0.76)	
> 60	104	52	33.3		0.72 (0.42 - 1.22)	
APACHE II				<0.0001		NS
Up to 11	163	43	20.9		1.00	
> 11	113	82	42.1		2.75 (1.77 - 4.27)	
ReOTI				<0.0001*		
No	273	96	26.0		1.00	1.00
Yes	3	29	90.6		27.49 (8.19 - 92.30)	13.15 (3.36 - 51.43)
IMV time (days)				<0.0001*		NS
< 7 days	103	32	23.7		1.00	
≥ 7 days	2	73	97.3		117.48 (27.29 - 505.74)	
Tracheostomy				<0.0001		
No	270	76	22.0		1.00	1.00
Yes	6	49	89.1		29.01 (11.97 - 70.31)	13.27 (4.89 - 35.99)

Chi-square test; *Fisher's exact test; stepwise logistic regression; NS – non-significant; IMV – invasive mechanical ventilation; ReOTI – orotracheal reintubation; APACHE II - Acute Physiology and Chronic Health Evaluation.

ference was found for gender. Patients between 40 and 60 years of age stayed longer in the intensive care unit as compared with younger or older patients (OR 0.43; 95%CI 0.25-0.76; *P*=0.01) (Table 6).

APACHE II score > 11 (OR 2.75; 95%CI 1.77-4.27; *P*<0.0001), ReOTI (OR 27.49; 95%CI 8.19-92-30; *P*<0.0001) and/or tracheostomy (OR 29.01; 95%CI 11.97-70.31; *P*<0.0001) (Table 6) were significantly associated with prolonged ICU time of stay.

DISCUSSION

We considered as prolonged ICU stay a patient remaining in the ICU longer than seven days, however we could not identify any literature consensus with ranging averages, e.g., 3 days,[2] 7 days,[8,9] 10 days,[10] 14 days,[5,11] or 30 days.[12,13] It is understood that this lack of literature consensus is probably due to most of the studies were conducted in mixed populations (i.e. both clinical and surgical patients). New studies ought to be conducted with better group characterization.

In the unit analyzed, a higher number of men were admitted. However, no significant difference regarding both mortality and prolonged stay between the genders was identified. Most of the studies confirm these data.[2-4,11] Only Fowler *et al.*[14] found a higher mortality rate in women.

In this study the mean age was 53.8± 18,0 years without significant difference identified for the admission of age groups. Mortality was proved to be higher in the group of patients between 40 and 60 years of age. Some studies identified advanced age to be associated with higher mortality rates, however these may have been influenced by other variables as they had small samples.[3,15] In a larger population study the mortality risk was not found to be associated with age.[10] Perhaps the effect of age on prognosis may be associated with other issues, such as disease severity and previous functional status.[3,16]

Prognosis indicators are being increasingly used for ICU quality assessment, comparison to other ICUs, or patient's randomization for clinical trial protocols. The APACHE II severity score assesses variables such as clinical, physiological and laboratory parameters as well as chronic disease and age, within the first 24 hours from admission.[17] Higher APACHE II scores are related to higher risks of death. The mean

APACHE II score, in literature, ranges from 12.8 to 24.9,[5,11,12,18] and in this study the APACHE II score averaged 12.0. Patients with APACHE II score above 11 had increased mortality and longer ICU stays, confirming the findings by Laupland et al.[5] It is understood that this prognostic instrument should be deemed just one additional tool for a doctor facing difficult decisions regarding therapeutic limitation or ICU beds distribution.

IMV is another factor considered to be associated with mortality risk and ICU length of stay.[11,13,18-20] According to the National Association for Medical Direction of Respiratory Care (NAMDRC) 2004 consensus,[21] the recent increase of number of patients undergoing prolonged time of mechanical ventilation is due to improved ICU care and technological evolution. An international prospective study reported that patients who required IMV remained in average 7 days under respiratory support, with 13 days ICU length of stay.[22] This study displayed that that 50% of patients who were not extubated within the first 24 hours stayed longer than 7 days in the ICU. Similar results were reported by Higgins *et al.*[23], in which mechanical ventilation was associated with infection and long ICU stay. IMV is then believed to indicate worse prognosis and that the longer it is maintained, the longer a patient's ICU stay will be.

The literature has stated that the use of protocols for IMV weaning managed by a multi-professional team, may significantly reduce IMV duration and consequently reduce the ICU length of stay.[24,25] The ICU should have an appropriately sized and trained multi-professional team, daily visit structured checklist focusing on the patient's eligibility for mechanical ventilation weaning.[26] Nisim *et al.*[27] in a recent study found that 95.3% of pre-extubation protocol patients were successfully extubated, while those not included in the protocol had increased ICU length of stay.

This study identified worse prognosis and prolonged ICU stay time for unsuccessful extubation patients. Caroleo *et al.*[28] observed that among people whose ages are over 70 years, pre-extubation mechanical ventilation time, anemia (hemoglobin (Hb) < 10 g/dL and hematocrit (Ht) > 30%), disease severity by the time of extubation, use of continued infusion sedation and patient's transportation out of the ICU may have the risk of reintubation increased. In a study by Esteban *et al.*[22] patients undergoing unplanned or accidental extubation had worse prognosis. Studies have described increased mortality and ICU length of stay up to 9 days for reintubated patients.[29,30] However, Ferrer,[31] in a systematic literature review, states that non-invasive mechanical ventilation immediately after extubation may be effective for post-extubation respiratory failure prevention in complication-risk patients specially those with chronic respiratory disorders or hypercapnic respiratory failure. Although our study has collected the causes leading to reintubation, our data are not sufficient to describe the variables which may have influenced the reintubation rates. New studies ought to be supported .

Patients requiring prolonged IMV, whose clinical status does not allow weaning, may undergo upper airways tracheostomy for protection. This type of cannulation may facilitate mechanical ventilation weaning as it reduces dead spaces and upper airways resistance, improves pulmonary secretions removal and reduces sedation requirements; nevertheless controlled studies on this subject are scarce.[32] Rumbak *et al.*[33] is one of the few randomized clinical trials in the literature on tracheostomy, showing mortality, incidence of pneumonia, ICU length of stay, and mechanical ventilation time benefits in early tracheostomy patients (within the first 48 hours under OTI) versus conventional tracheostomy (after 14 days OTI). However, this study has shown that tracheostomyzed patients have displayed increased mortality in agreement with the findings by Colpan *et al.*[18] and longer ICU stay time; nonetheless, these data should be reassessed taking into consideration the tracheostomy time (early/late), mechanical ventilation days and other variables.

CONCLUSION

It is possible to conclude that in this study APACHE II > 11, tracheostomy and reintubation were associated with increased mortality rate and prolonged ICU stay.

RESUMO

Objetivo: A unidade de terapia intensiva é sinônimo de gravidade e apresenta taxa de mortalidade entre 5,4% e 33%. Com o aperfeiçoamento de novas tecnologias, o paciente pode ser mantido por longo período nessa unidade, ocasionando altos custos financeiros, morais e psicológicos para todos os envolvidos. O objetivo do presente estudo foi avaliar os fatores associados à maior mortalidade e tempo de internação prolongado em uma unidade de terapia intensiva adulto.

Métodos: Participaram deste estudo todos os pacientes ad-

mitidos consecutivamente na unidade de terapia intensiva de adultos, clínica/cirúrgica do Hospital das Clínicas da Universidade Estadual de Campinas, no período de seis meses. Foram coletados dados como: sexo, idade, diagnóstico, antecedentes pessoais, APACHE II, dias de ventilação mecânica invasiva, reintubação orotraqueal, traqueostomia, dias de internação na unidade de terapia intensiva, alta ou óbito na unidade de terapia intensiva.

Resultados: Foram incluídos no estudo 401 pacientes, sendo 59,6% homens e 40,4% mulheres, com idade média de 53,8±18,0 anos. A média de internação na unidade de terapia intensiva foi de 8,2±10,8 dias, com taxa de mortalidade de 13,46%. Dados significativos para mortalidade e tempo de internação prolongado em unidade de terapia intensiva (p<0,0001), foram: APACHE II >11, traqueostomia e reintubação.

Conclusão: APACHE >11, traqueostomia e reintubação estiveram associados, neste estudo, à maior taxa de mortalidade e tempo de permanência prolongado em unidade de terapia intensiva.

Descritores: Unidade de terapia intensiva; Mortalidade; Tempo de internação; Fatores de risco

REFERENCES

1. São Paulo. Conselho Regional de Medicina do Estado de São Paulo. Resolução CREMESP nº 170, de 6 de novembro de 2007**.** Define e regulamenta as atividades das Unidades de Terapia Intensiva. Diário Oficial do Estado de São Paulo; Poder Executivo, 22 nov 2007. Seção 1, p. 152.
2. Abelha FJ, Castro MA, Landeiro NM, Neves AM, Santos CC. Mortalidade e o tempo de internação em uma unidade de terapia intensiva cirúrgica. Rev Bras Anestesiol. 2006;56(1):34-45.
3. Williams TA, Dobb GJ, Finn JC, Webb SA. Long-term survival from intensive care: a review. Intensive Care Med. 2005;31(10):1306-15.
4. Friedrich JO, Wilson G, Chant C. Long-term outcomes and clinical predictors of hospital mortality in very long stay intensive care unit patients: a cohort study. Crit Care. 2006;10(2):R59.
5. Laupland KB, Kirkpatrick AW, Kortbeek JB, Zuege DJ. Long-term mortality outcome associated with prolonged admission to the ICU. Chest. 2006;129(4):954-9.
6. Orlando JMC, Milani CJ. 2º Anuário Brasileiro de UTIs – 2º Censo Brasileiro de UTIs. São Paulo: Associação de Medicina Intensiva Brasileira (AMIB); Edição 2002-2003.
7. Moritz RD, Schwingel RF, Machado FO. Critérios prognósticos de pacientes graves: comparação entre a percepção dos médicos e o índice APACHE II. Rev Bras Ter Intensiva. 2005;17(3):176-80.
8. Stricker K, Rothen HU, Takala J. Resource use in the ICU: short- vs. long-term patients. Acta Anaesthesiol Scand. 2003; 47(5):508-15.
9. Lipsett PA, Swoboda SM, Dickerson J, Ylitalo M, Gordon T, Breslow M, et al. Survival and functional outcome after prolonged intensive care unit stay.
10. Williams TA, Ho KM, Dobb GJ, Finn JC, Knuiman M, Webb SA; Royal Perth Hospital ICU Data Linkage Group. Effect of length of stay in intensive care unit on hospital and long-term mortality of critically ill adult patients. Br J Anaesth. 2010;104(4):459-64.
11. Arabi Y, Venkatesh S, Haddad S, Al Shimemeri A, Al Malik S. A prospective study of prolonged stay in the intensive care unit: predictors and impact on resource utilization. Int J Qual Health Care. 2002;14(5):403-10.
12. Hughes M, MacKirdy FN, Norrie J, Grant IS. Outcome of long-stay intensive care patients. Intensive Care Med. 2001;27(4):779-82.
13. Santana Cabrera L, Sánchez-Palacios M, Hernández Medina E, Eugenio Robaina P, Villanueva-Hernández A. [Characteristics and prognosis of patients with very long stay in an Intensive Care Unit]. Med Intensiva. 2008;32(4):157-62. Spanish.
14. Fowler RA, Sabur N, Li P, Juurlink DN, Pinto R, Hladunewich MA, et al. Sex-and age-based differences in the delivery and outcomes of critical care. CMAJ. 2007;177(12):1513-9.
15. Boumendil A, Somme D, Garrouste-Orgeas M, Guidet B. Should elderly patients be admitted to the intensive care unit? Intensive Care Med. 2007;33(7):1252-62. Review.
16. de Rooij SE, Abu-Hanna A, Levi M, de Jonge E. Factors that predict outcome of intensive care treatment in very elderly patients: a review. Crit Care. 2005;9(4):R307-14.
17. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med. 1985;13(10):818-29.
18. Colpan A, Akinci E, Erbay A, Baladan N, Bodur H. Evaluation of risk factors for mortality in intensive care units: a prospective study from a referral hospital in Turkey. Am J Infect Control. 2005;33(1):42-7.
19. Combes A, Costa MA, Trouillet JL, Baudot J, Mokhtari M, Gilbert C, Chastre J. Morbidity, mortality, and quality-of-life outcomes of patients requiring >or= 14 days of mechanical ventilation. Crit Care Med. 2003;31(5):1373-81.
20. Zilberberg MD, Kramer AA, Higgins TL, Shorr AF. Prolonged acute mechanical ventilation: implications for hospital menchmarking. Chest. 2009;135(5):1157-62.
21. MacIntyre NR, Epstein SK, Carson S, Scheinhorn D, Christopher K, Muldoon S; National Association for Medical Direction of Respiratory Care. Management of patients requiring prolonged mechanical ventilation: report of a NAMDRC consensus conference. Chest. 2005;128(6):3937-54.

22. Esteban A, Anzueto A, Frutos F, Alía I, Brochard L, Stewart TE, Benito S, Epstein SK, Apezteguía C, Nightingale P, Arroliga AC, Tobin MJ; Mechanical Ventilation International Study Group. Characteristics and outcomes in adult patients receiving mechanical ventilation: a 28-day international study. JAMA. 2002;287(3):345-55.
23. Higgins TL, McGee WT, Steingrub JS, Rapoport J, Lemeshow S, Teres D. Early indicators of prolonged intensive care unit stay: impact of illness severity, physician staffing, and pre-intensive care unit length of stay. Crit Care Med. 2003;31(1):45-51.
24. Kollef MH, Shapiro SD, Silver P, St John RE, Prentice D, Sauer S, et al. A randomized, controlled trial of protocol-directed versus physician-directed weaning from mechanical ventilation. Crit Care Med. 1997;25(4):567-74.
25. Tonnelier JM, Prat G, Le Gal G, Gut-Gobert C, Renault A, Boles JM, L'Her E. Impact of a nurses' protocol-directed weaning procedure on outcomes in patients undergoing mechanical ventilation for longer than 48 hours: a prospective cohort study with a matched historical control group. Crit Care. 2005;9(2):R83-9.
26. Goldwasser R, Farias A, Freitas EE, Saddy F, Amado V, Okamoto V. Desmame e interrupção da ventilação mecânica. J Bras Pneumol. 2007;33(Supl 2):128-36.
27. Nisim AA, Margulies DR, Wilson MT, Alban RF, Dang CM, Allins AD, Shabot MM. A 2-minute pre-extubation protocol for ventilated intensive care unit patients. Am J Surg. 2008;196(6):890-4; discussion 894-5.
28. Caroleo S, Agnello F, Abdallah K, Santangelo E, Amantea B. Weaning from mechanical ventilation: an open issue. Minerva Anestesiol. 2007;73(7-8):417-27.
29. Seymour CW, Martinez A, Christie JD, Fuchs BD. The outcome of extubation failure in a community hospital intensive care unit: a cohort study. Crit Care. 2004;8(5):R322-7.
30. Arabi Y, Haddad S, Shirawi N, Al Shimemeri A. Early tracheostomy in intensive care trauma patients improves resource utilization: a cohort study and literature review. Crit Care. 2004;8(5):R347-52.
31. Ferrer M. Non-invasive ventilation in the weaning process. Minerva Anestesiol. 2008;74(6):311-4.
32. Pierson DJ. Tracheostomy and weaning. Respir Care. 2005;50(4):526-33.
33. Rumbak MJ, Newton M, Truncale T, Schwartz SW, Adams JW, Hazard PB. A prospective, randomized, study comparing early percutaneous dilational tracheotomy to prolonged translaryngeal intubation (delayed tracheotomy) in critically ill medical patients. Crit Care Med. 2004;32(8):1689-94. Erratum in: Crit Care Med. 2004;32(12):2566.