



Delirium recognition and sedation practices in critically ill patients: A survey on the attitudes of 1015 Brazilian critical care physicians[☆]

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Acute brain dysfunction

Abstract

Purpose: The aim of the study was to characterize the practices of Brazilian ICU physicians toward sedation and delirium.

Materials and Methods: A cross-sectional survey was conducted among a convenience sample of critical care physicians between April and June 2008.

Results: One thousand fifteen critical care physicians responded. Sedation scoring systems were used by 893 (88.3%) of the respondents. The Ramsay and Richmond Agitation-Sedation Scale were used by 81.9% and 6.8% of the respondents, respectively. Most respondents did not discuss sedation targets (62.8%) or practice daily sedative interruption (68.3%) in most patients. More than half of the respondents (52.7%) used a sedation protocol, and the most used sedatives were midazolam (97.8%), fentanyl (91.5%), and propofol (55%). A significant rate of the respondents (42.7%) estimated that more than 25% of

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patients under mechanical ventilation have delirium, but 53.5% occasionally assessed patients for delirium. Thirteen percent used specific delirium scales, with the Confusion Assessment Method for intensive care unit (ICU) being the most applied. Delirium was often treated with haloperidol (88.1%); however, atypical antipsychotics (36.3%) and benzodiazepines (42.3%) were also used.

Conclusions: Despite the recent advances in knowledge of sedation and delirium, most of them are still not translated into clinical practice. Significant variation in practice is observed among ICU physicians and represents a potential target for future research and educational interventions.

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1. Introduction

Critically ill patients frequently need invasive procedures and require several forms of advanced life support, especially mechanical ventilation (MV). Sedatives and analgesics are often used in mechanically ventilated patients to improve patient ventilator synchrony and to relieve anxiety and physical distress. However, in recent years, there is increasing evidence that excessive sedation is associated with longer duration of mechanical ventilation [1] and longer intensive care unit (ICU) length of stay [2]. Oversedation is associated with slower awakenings, more neurologic investigations for coma [2], and long-term neuropsychiatric dysfunction [3-5]. Delirium is a form of acute brain dysfunction that occurs in up to 80% of mechanically ventilated patients and is a strong predictor of adverse outcomes in critically ill patients [6]. Moreover, several neurologic events that occur in ICU patients maybe ascribed to specific sedation regimens [2,7]. The use of benzodiazepines has been recently associated with the occurrence of transitioning delirium [8,9] and the use of drug-regimens that are based on avoidance of benzodiazepines [8] or on the use of α -2 agonists [7] may result in increased delirium-free days. The Society of Critical Care Medicine (SCCM) guidelines for sedation and analgesia [1] recommends the use of sedation scales, daily sedative interruptions, and delirium monitoring for optimal patient care. However, it remains unclear how these recommendations have translated into clinical practice. In view of this increasing knowledge in the field, we conducted a national survey of Brazilian ICU physicians to determine the perceived use of sedation scoring systems; daily interruption and goal-directed sedation; and delirium assessment, monitoring, and treatment.

2. Methods

2.1. Survey development and administration

We conducted a Medline search of the literature on “sedation,” “delirium,” “mechanical ventilation,” and “ICU” to identify the most important aspects in the field that could facilitate the development of the questionnaire’s

items. We also surveyed the members of the Brazilian Research in Intensive Care Network steering committee to identify other potential domains of interest.

This resulted in a 3-part questionnaire that evaluated the respondents and related ICU profile (10 questions), sedation practices (14 questions), and delirium assessment and management (10 questions). The format of the questionnaire was mainly of tick boxes.

This questionnaire was answered by ICU physicians and medical students at the Instituto Nacional de Câncer (Rio de Janeiro, Brazil). After these responses and critical inputs, a second evaluation of the survey’s contents was performed by the authors (FP, JIFS, MS, and FAB). This resulted in the final version of a self-administered questionnaire constructed on a Web-based system (www.surveymonkey.com). The survey did not contain data that could identify the responders. The institutional review board approved the study and waived the need for informed consent.

From April 1 until May 31, 2008, an invitation to take part in the survey with the respective Web link was sent by email to a convenience sample of ICU physicians using the mailing list of Associação de Medicina Intensiva Brasileira (Brazilian Society of Intensive Care Medicine). Computers were also available for response during the Brazilian Congress of Intensive Care (May 8-10, 2008). The active link was also available on the Brazilian Society of Intensive Care Medicine ([Associação de Medicina Intensiva Brasileira; www.amib.com.br](http://www.amib.com.br)) and on the Brazilian Research in Intensive Care Network (www.bricnet.org) Web sites. Physicians were instructed not to complete the survey again, if they had already answered it before.

2.2. Data and statistical analysis

The survey results were exported into a Microsoft Excel template and analyzed using the statistical package Prism 3.0 (Graphpad Software California, USA). Standard descriptive statistics were used as appropriate. Variables were reported as number (percentage). As the number of respondents varied across the questions, the proportions displayed in the results section and tables were not constant. Fischer exact test was used for the comparison of the variables. A 2-sided *P* value of less than .05 was considered significant.

3. Results

3.1. Demographics

A total of 1015 critical care physicians responded to the survey. The main respondents' demographics and ICU characteristics are depicted in Table 1. We had responders from all geographic regions of the country, and every state was represented in our sample. Among all physicians who browsed the survey, 76% provided complete responses and had their results analyzed. Among the respondents, 539 (49.4%) were board-certified critical care physicians, whereas the remaining 552 (50.6%) had profession of other specializations, mainly internal medicine, anesthesiology, pulmonary medicine, and surgery.

3.2. Sedation practices

Most respondents reported the use of some sedation scale (n = 883; 88.3%). Just more than half of the respondents reported performance of daily interruptions of sedation (n = 578; 57.2%), and wide variation in the extent of its application was observed (Table 2). Attitudes of ICU physicians toward sedation are detailed in Table 2. Drug regimens varied widely (Fig. 1), but most physicians administered a combination of midazolam (n = 989; 97.8%) and fentanyl (n = 925; 91.5%) for sedation.

A written protocol for sedation was available for 533 (52.7%) of the respondents, though these were system-

Table 2 Attitudes toward sedation management

	n (%)
Sedation scoring system ^a	
None	116 (11.5)
Ramsay	828 (81.9)
RASS	69 (6.8)
SAS	53 (5.2)
No. of times sedation level is assessed (per day)	
<1	46 (4.5)
1	217 (21.5)
2	374 (37)
3	220 (21.8)
>3	154 (15.2)
Written sedation protocol	
Has written sedation protocol	533 (52.7)
No written sedation protocol	478 (47.3)
Estimate % times daily sedation goals are discussed	
Never	114 (11.3)
<25	253 (25)
25-50	268 (26.5)
50-75	145 (14.3)
>75	231 (22.8)
Estimate % times daily interruption of sedation is performed	
Never	213 (21.1)
<25	239 (23.6)
-50	239 (23.6)
50-75	147 (14.5)
>75	173 (17.1)

RASS indicates Richmond Agitation-Sedation scale; SAS, Sedation Agitation Scale.

^a Respondents could choose more than one answer.

Table 1 Demographics of the survey responders

	n (%)
Years of practice (n)	
1-5	324 (29.3)
6-10	266 (24.1)
>10	515 (46.6)
Main practice setting	
Academic medical center	217 (19.6)
Nonacademic medical center	888 (80.4)
No. of ICU beds	
1-10	465 (42.1)
11-20	452 (40.9)
≥20	188 (17)
Estimate % of patients under mechanical ventilation	
<20	49 (4.4)
20-40	277 (25.1)
40-70	515 (46.6)
>70	264 (23.9)
Daily multidisciplinary rounds in the ICU ^a	
Has daily rounds	872 (86.3)
No daily rounds	139 (13.7)

^a "n" does not equal to 1015 because not all respondents answered this question.

atically applied by only 212 (21.2%) of ICU physicians. Most physicians also agreed that patients were usually oversedated (n = 776; 85.6%).

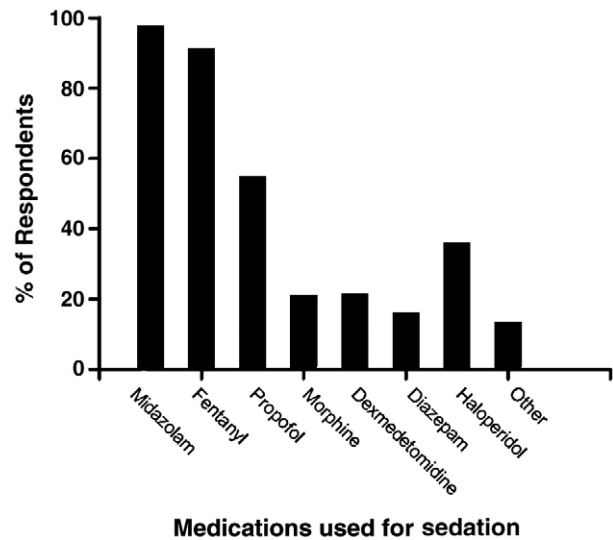


Fig. 1 Medications used for sedation management. This histogram shows the use of medications for the management of sedation. A total of 1011 physicians answered this question. More than one drug could be mentioned by each physician.

Table 3 Attitudes toward delirium assessment and management

	n (%)
Delirium evaluation ^a	
Clinical evaluation	828 (91.3)
Ramsay	91 (10.0)
RASS	19 (2.1)
SAS	11 (1.2)
No. of times delirium is assessed (per day)	
<1	348 (38.4)
1	244 (26.9)
2	181 (20.0)
3	91 (10.0)
>3	43 (4.7)
Estimate % of delirium prevalence in mechanically ventilated patients	
<10	128 (14.1)
10-25	301 (33.2)
25-50	330 (36.4)
50-75	120 (13.2)
>75	28 (3.1)
Estimate % of delirium prevalence in nonmechanically ventilated patients	
<10	184 (20.3)
10-25	392 (43.2)
25-50	242 (26.7)
50-75	82 (9.0)
>75	7 (0.8)

Please refer to [Table 2](#) for abbreviations used.

^a Respondents could choose more than one answer.

We asked physicians for their opinion on 6 strategies to improve sedation practices. Most physicians agreed or strongly agreed that written protocols ($n = 945$; 93.4%), the use of a standard sedation scale ($n = 939$; 92.8%), and routine monitoring of sedation levels ($n = 979$; 96.8%) are useful strategies to improve sedation practices. Also, most physicians agreed or strongly agreed that training nurses ($n = 857$; 84.8%) and physicians ($n = 963$; 95.2%) for routine monitoring of sedation is useful. However, only 396 (38.9%) of the respondents felt that a pharmacist in the daily rounds could lead to improvement in the quality of sedation.

3.3. Delirium assessment and management

The respondents described which components are necessary for the diagnosis of delirium in their opinion as follows: fluctuating level of consciousness ($n = 868$; 85.9%), agitation ($n = 960$; 95%), inattention ($n = 825$; 81.6%), hallucinations ($n = 903$; 89.3%), disorganized thinking ($n = 960$; 95%), and recent onset of symptoms ($n = 884$; 87.4%). Most physicians were aware of the existence of delirium scales validated for the use in ICU patients ($n = 581$; 64%). Nonetheless, a significant number of physicians ($n = 828$; 91.3%) relied on the clinical evaluation for the assessment of delirium (detailed data on [Table 3](#)). Most respondents agreed or strongly agreed that delirium is an underdiagnosed condition ($n = 851$; $n =$

83.9%), usually present in critically ill patients ($n = 671$; 74%) that requires an intervention ($n = 776$; 68.3%). Most physicians also agreed or strongly agreed that delirium is a preventable complication ($n = 619$; 67.3%), whose occurrence is associated with sedation strategies ($n = 741$; 81.7%) and that it represents an independent risk factor for prolonged mechanical ventilation ($n = 850$; 93.8%) and ventilator-associated pneumonia ($n = 722$; 79.6%) thus increasing the risk of death especially in the elderly ($n = 717$; 79%).

Facing a patient with delirium, most physicians will use haloperidol (88.1%), but at a significant number of times (44.2%), benzodiazepines and atypical antipsychotic agents (36%) were considered as treatment options ([Fig. 2](#)).

3.4. Comparisons among academic and nonacademic institutions and among specialists and nonspecialists in critical care

We performed comparisons among ICU physicians working at academic and nonacademic institutions. Physicians from academic institutions more often were board certified in critical care (128 [59.3%] vs 411 [46.9%]; $P = .001$). No differences were observed regarding the number of years of practice (<10 years: 117 [53.9%] vs 472 [53.2%]; $P = .87$). Similar use of sedation scales were reported (87.7% for academic vs 87.1% for nonacademic ICUs; $P = .71$); the Ramsay scale was the most often used (80% by academic vs 82.2% by nonacademic ICUs; $P = .41$), and sedation levels were assessed less than twice a day by most physicians (72.2% for academic vs 62.5% for nonacademic ICUs; $P = .15$). However, sedation targets were more often discussed by physicians in academic institutions as compared to nonacademic institutions (117 [87.1%] vs 518 [63.4%]; $P = .001$).

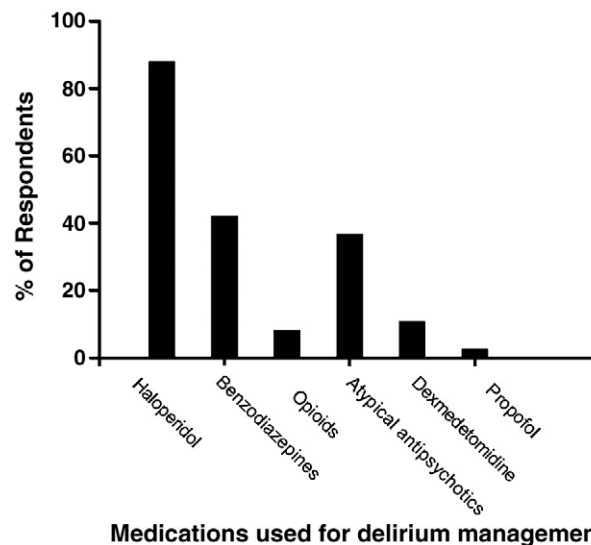


Fig. 2 Medications used for delirium management. This histogram shows the use of medications for the management of delirium. A total of 907 physicians answered this question. More than one drug could be mentioned by each physician.

A written sedation protocol was reported to be available by a similar proportion of the respondents (52.8% for academic vs 52.8% for nonacademic ICUs; $P = .99$). No differences in daily interruption of sedation were reported though it occurred in less than 50% of patients on MV (71.2% for academic vs 66.4% for nonacademic ICUs; $P = .2$). Regarding the therapeutic regimens, the only observed differences were related to a more frequent use of morphine in academic ICUs (55 [28.2%] vs 158 [19.3%]; $P = .008$) and a less frequent report of use of dexmedetomidine in academic centers (28 [14.4%] vs 191 [23.4%]; $P = .003$).

Physicians from academic and nonacademic ICUs reported similar patterns of perception and practice regarding delirium. Most estimated that more than 25% of the patients undergoing MV had delirium (104 [57.7%] vs 374 [51.4%]; $P = .15$) and used the general clinical evaluation for the detection of delirium (167 [92.8%] vs 661 [90.9%]; $P = .55$). The Confusion Assessment Method for ICU was reported to be used in a similar proportion by respondents from academic and nonacademic institutions (18 [10%] vs 73 [10.1%]; $P = .99$), and the frequency of screening for delirium was also similar being performed less than twice a day by most physicians in both settings (68.8% vs 64.3%; $P = .29$). The pharmacologic interventions for delirium were comparable for the 2 groups except for a less frequent use of atypical antipsychotics by physicians in academic institutions (51 [28.3%] vs 284 [34.8%]; $P = .003$).

We performed the same comparisons among board-certified critical care physicians and physicians without the specialist certification but who worked in ICUs. Comparable responses were observed in all domains. The only few different aspects were related to the number of years of practice, use of sedatives, and daily interruption of sedation. More critical care specialists had a practice in the ICU for longer than 10 years as compared to nonspecialists (387 [71.8%] vs 119 [21.6%]; $P = .0002$). Critical care specialists reported to use morphine more often than nonspecialists (132 [26.4%] vs 83 [16.7%]; $P = .0002$), had a trend toward more use of dexmedetomidine (121 [24.2%] vs 95 [19.1%]; $P = .054$), and performed more daily interruption of sedation (301 [60.2%] vs 270 [54.2%]; $P = 0.06$). The ICUs where these critical care specialists worked had a higher proportion of written sedation protocols as compared to those of nonspecialists (303 [60.6%] vs 221 [44.4%]; $P = .0001$). However, perceived practices regarding delirium were comparable in all aspects.

4. Discussion

We conducted a national survey aiming to characterize the perceived attitudes of Brazilian ICU physicians toward diagnosis, monitoring, and pharmacologic interventions for delirium and sedation.

More than 5 years ago, the 2002 practice parameters for sedations and analgesia of the SCCM already highlighted the

importance of sedation monitoring using specific scales and also regarding the choice of sedatives [1]. Moreover in recent years, several studies demonstrated that delirium is frequent in critically ill patients, especially in those on MV and that its occurrence is associated with longer ICU stay, elevated costs, and increased mortality rates [6,10]. In addition, recent studies have demonstrated that sedation strategies maybe associated with higher rates of delirium [7,8]. Despite this significant increase in the current knowledge on delirium and sedation, information on how it translates to clinical practice is scarce. Actually, recent studies demonstrate that advances in the current knowledge of caring for critically ill patients are often translated into practice [11], but this may take several years even in academic institutions [12]. The results of the present survey reveal a significant gap between physicians' knowledge on sedation and delirium and their practical attitudes.

The use of validated sedation scales is strongly recommended (grade B) [1]. Different surveys have demonstrated that less than 50% of physicians report using sedation protocols [13,14], but the more recently conducted evaluation [15] shows an increasing compliance to those strategies as compared to data obtained in a previous survey [6]. A recently published survey indicates that most United Kingdom ICUs use a sedation guideline and sedation scoring tool [16]. The concept of sedation holding has been implemented in most units, and most ICUs have a written sedation guideline [16]. In the current survey, most respondents (88.3%) reported the use of some sedation scoring system; however, the reported frequency of sedation monitoring is clearly insufficient. The same may be concluded about sedation protocols as most physicians (85.6%) agreed that patients are usually over-sedated, and most respondents (52.7%) have a written sedation protocol. However, it is only systematically applied by 21.2% of ICU physicians. Such discrepancies are present in several aspects regarding sedation and delirium. The 2002 SCCM guidelines grade recommends the use of daily sedation interruption (grade A). In our survey, only 37.1% of the respondents used daily interruption in more than 50% of the mechanically ventilated patients. Several studies demonstrate that using daily interruption of sedatives is associated with reduced duration of MV, improved in-hospital outcomes [2,7], and post-ICU neuropsychologic consequences [3,17]. However, there may be several barriers to implement protocols and daily interruption of sedation on a regular basis, and these are organizational issues and a feeling of uncertainty regarding safety of the interruption by the assistant physicians. Regarding the types of sedatives, it is interesting to observe that the most commonly used drugs are midazolam and fentanyl. Lorazepam is not available as the intravenous formulation in Brazil; this may explain some of the differences when compared to the North American [15] and Canadian surveys [13]. Pharmacologic interventions for delirium are mostly based on haloperidol (>85% of

responders) but also include other drug classes as benzodiazepines, opioids, dexmedetomidine, and atypical antipsychotics. This is an important target for medical education as benzodiazepines are associated with increased risk of delirium. The mentioned use of both haloperidol and atypical antipsychotics were not tested in prospective randomized controlled trials represents an interesting field for future investigation. Interestingly, although few studies to date systematically addressed this issue, there is a perception among respondents that delirium is a preventable complication.

In the present survey, we also could observe that validated sedation scoring systems are widely, although insufficiently, applied. However, delirium screening and evaluation is an even more worrisome issue. Despite the recognition of the importance of delirium as a serious clinical condition associated with adverse outcomes, less than 15% of the respondents use a validated delirium assessment tool, and most rely solely on clinical evaluation and often (65.3%) screen the patients for the presence of delirium less than twice a day. Moreover, a significant number of respondents believe that agitation is an essential component for the diagnosis. According to a recent survey, Canadian intensivists seldom screen patients for delirium [13]. More recently, a survey of North American health care professionals showed more promising results as the reported prevalence of delirium screening was 59% [15]. Nevertheless, similarly to what we observed, most health care professionals in the United States and Canada still use the general clinical evaluation for the detection of delirium [13]. Studies demonstrate that clinical evaluation may fail to recognize delirium in critically ill patients, especially the hypoactive subtype [17-19]. Moreover, there is significant variation in the diagnosis of delirium among ICU physicians [20]. Actually, according to recent surveys, the use of validated systems as the Confusion Assessment Method for ICU vary from less than 8% in Canada [13,21] to 10% among Brazilian ICU physicians up to 24% in the North American survey [15]. In our study, most physicians reported that hallucinations and agitation were necessary components for the diagnosis of delirium.

This only confirms the notion that delirium and acute brain dysfunction are emerging areas of knowledge where much effort is needed to unify the present definitions [21] and increase the data on pathophysiology [22-24], epidemiology [9,17,18], and possible interventions [7,25].

Interestingly, physicians working in nonacademic and academic institutions had a similar pattern of practice; however, when we compared those who were specialists in critical care with nonspecialists who worked in critical care, differences were observed. Most differences were related to sedation practices (specialists more frequently used of morphine and dexmedetomidine and had a tendency to perform more daily interruption of sedation). However, once again this was not extensive to better monitoring or treatment of delirium. It is worth mentioning that most

ICUs are not in university and academic centers in Brazil; therefore, it is expected to have fewer respondents affiliated with such institutions.

The present survey has several limitations. As in any survey, we acknowledge that the possible occurrence of inaccuracies due to poor recollection may result in discrepancies between the reported and the actual practice. Selection bias may have occurred as we have used the society of intensive care Web site and medical congress to enroll physicians. It is reasonable to assume that those attending intensive care conferences would be more prone to being up to date than other physicians. In addition, selection bias may have occurred due to the length of the survey; however, global respondent rate was high (76%), and the sample involved physicians from all geographic regions of the country.

5. Conclusion

In conclusion, this survey provides valuable data on the perceived attitudes of Brazilian ICU physicians regarding sedation and delirium. Although delirium is acknowledged by most respondents as a severe medical condition, few systematic tools are used in clinical practice for the evaluation and treatment of delirium. Moreover, although daily interruption of sedation is a well-known concept and sedation scales are often used by the respondents, insufficient effort is put into frequent monitoring, use of protocols, and systematic implementation of sedation strategies. The results of the present survey reemphasize the need to implement widespread educational efforts for the implementation of evidence-based strategies for the use of sedatives and the detection, monitoring, and treatment of delirium in ICU patients.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jrcr.2009.04.004.

References

- [1] Jacobi J, Fraser GL, Coursin DB, et al. Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. *Crit Care Med* 2002;30:119-41.
- [2] Kress JP, Pohlman AS, O'Connor MF, et al. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *N Engl J Med* 2000;342:1471-7.
- [3] Kress JP, Gehlbach B, Lacy M, et al. The long-term psychological effects of daily sedative interruption on critically ill patients. *Am J Respir Crit Care Med* 2003;168:1457-61.
- [4] Girard TD, Shintani AK, Jackson JC, et al. Risk factors for post-traumatic stress disorder symptoms following critical illness requiring mechanical ventilation: a prospective cohort study. *Crit Care* 2007;11:R28.
- [5] Jackson JC, Hart RP, Gordon SM, et al. Post-traumatic stress disorder and post-traumatic stress symptoms following critical illness in medical intensive care unit patients: assessing the magnitude of the problem. *Crit Care* 2007;11:R27.
- [6] Ely EW, Shintani A, Truman B, et al. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. *JAMA* 2004;291:1753-62.
- [7] Pandharipande PP, Pun BT, Herr DL, et al. Effect of sedation with dexmedetomidine vs lorazepam on acute brain dysfunction in mechanically ventilated patients: the MENDS randomized controlled trial. *JAMA* 2007;298:2644-53.
- [8] Pandharipande P, Shintani A, Peterson J, et al. Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. *Anesthesiology* 2006;104:21-6.
- [9] Pandharipande P, Cotton BA, Shintani A, Thompson J, Pun BT, Morris Jr JA, Dittus R, Ely EW. Prevalence and risk factors for development of delirium in surgical and trauma intensive care unit patients. *J Trauma* 2008;65:34-41.
- [10] Milbrandt EB, Deppen S, Harrison PL, et al. Costs associated with delirium in mechanically ventilated patients. *Crit Care Med* 2004;32:955-62.
- [11] Esteban A, Ferguson ND, Meade MO, et al. Evolution of mechanical ventilation in response to clinical research. *Am J Respir Crit Care Med* 2008;177:170-7.
- [12] Weinert CR, Gross CR, Marinelli WA. Impact of randomized trial results on acute lung injury ventilator therapy in teaching hospitals. *Am J Respir Crit Care Med* 2003;167:1304-9.
- [13] Mehta S, Burry L, Fischer S, et al. Canadian survey of the use of sedatives, analgesics, and neuromuscular blocking agents in critically ill patients. *Crit Care Med* 2006;34:374-80.
- [14] Christensen BV, Thunborg LP. Use of sedatives, analgesics and neuromuscular blocking agents in Danish ICUs 1996/97. A national survey. *Intensive Care Med* 1999;25:186-91.
- [15] Patel RP, Gambrell M, Speroff T, Scott TA, Pun BT, Okahashi J, et al. Delirium and sedation in the intensive care unit (ICU): survey of behaviors and attitudes of 1,384 healthcare professionals. *Crit Care Med* 2009;37:825-32.
- [16] Reschreiter HP, Maiden MJ, Kapila A. Sedation practice in the intensive care unit: a UK national survey. *Crit Care* 2008;12:R152.
- [17] Ouimet S, Kavanagh BP, Gottfried SB, et al. Incidence, risk factors and consequences of ICU delirium. *Intensive Care Med* 2007;33:66-73.
- [18] Pandharipande P, Cotton BA, Shintani A, et al. Motoric subtypes of delirium in mechanically ventilated surgical and trauma intensive care unit patients. *Intensive Care Med* 2007;33:1726-31.
- [19] Ouimet S, Riker R, Bergeron N, et al. Subsyndromal delirium in the ICU: evidence for a disease spectrum. *Intensive Care Med* 2007;33:1007-13.
- [20] Cheung CZ, Alibhai SM, Robinson M, et al. Recognition and labeling of delirium symptoms by intensivists: does it matter? *Intensive Care Med* 2008;34:437-46.
- [21] Morandi A, Pandharipande P, Trabucchi M, et al. Understanding international differences in terminology for delirium and other types of acute brain dysfunction in critically ill patients. *Intensive Care Med* 2008.
- [22] d'Avila Jda C, Santiago AP, Amancio RT, et al. Sepsis induces brain mitochondrial dysfunction. *Crit Care Med* 2008;36:1925-32.
- [23] Ely EW, Girard TD, Shintani AK, et al. Apolipoprotein E4 polymorphism as a genetic predisposition to delirium in critically ill patients. *Crit Care Med* 2007;35:112-7.
- [24] Barichello T, Fortunato JJ, Vitali AM, et al. Oxidative variables in the rat brain after sepsis induced by cecal ligation and perforation. *Crit Care Med* 2006;34:886-9.
- [25] Devlin JW, Fong JJ, Schumaker G, et al. Use of a validated delirium assessment tool improves the ability of physicians to identify delirium in medical intensive care unit patients. *Crit Care Med* 2007;35:2721-4 [quiz 2725].