Anesthesiology 2002; 97:148–56

Impact of Unplanned Extubation and Reintubation after Weaning on Nosocomial Pneumonia Risk in the Intensive Care Unit

A Prospective Multicenter Study

Arnaud de Lassence, M.D., Corinne Alberti, M.D.,† Élie Azoulay, M.D.,‡ Eric Le Miere, M.D.,§ Christine Cheval, M.D.,‖ François Vincent, M.D.,# Yves Cohen, M.D.,** Maïté Garrouste-Orgeas, M.D.,†† Christophe Adrie, M.D.,‡‡ Gilles Troche, M.D.,§§ Jean-François Timsit, M.D.,‖‖ for the OUTCOMEREA Study Group##*

Background: **The authors prospectively evaluated the occurrence and outcomes of unplanned extubations (self-extubation and accidental extubation) and reintubation after weaning, and examined the hypothesis that these events may differ regarding their influence on the risk of nosocomial pneumonia.**

Methods: **Data were taken from a prospective, 2-yr database including 750 mechanically ventilated patients from six intensive care units.**

Results: **One hundred five patients (14%) experienced at least one episode of these 3 events; 51 self-extubations occurred in 38 patients, 24 accidental extubations in 22 patients, and 56 reintubations after weaning in 45 patients. The incidence density of these 3 events was 16.4 per 1,000 mechanical ventilation days. Reintubation within 48 h was needed consistently after accidental extubation but was unnecessary in 37% of self-extubated patients. Unplanned extubation and reintubation after weaning were associated with longer total mechanical ventilation (17 vs. 6 days; $P < 0.0001$), intensive care unit stay (22 *vs.* 9 days; $P < 0.0001$), and hospital stay (34 *vs.* 18 days; $P < 0.0001$) than in control group, but did not influence intensive care unit or hospital mortality. The incidence of nosocomial pneumonia was significantly higher in patients with unplanned extubation or reintubation after weaning (27.6% *vs.* 13.8%; $P = 0.002$). In a Cox model adjusting on severity at admission, unplanned extubation and reintubation after weaning increased the risk of nosocomial pneumonia (relative risk, 1.80; 95% confidence interval, 1.15–2.80; $P = 0.009$). This risk increase was entirely ascribable to accidental extubation (relative risk, 5.3; 95% confidence interval, 2.8–9.9; $P < 0.001$).**

Conclusion: **Accidental extubation but not self-extubation or reintubation after weaning increased the risk of nosocomial pneumonia. These 3 events may deserve evaluation as an indicator for quality-of-care studies.**

* Staff Physician, § Attending Physician, Medical ICU, Louis Mourier Teaching Hospital. † Staff Physician, Department of Biostatistics, U444-INSERM, Paris 7 University, Paris France. ‡ Staff Physician, ICU, Saint Louis Teaching Hospital. ‖ Staff Physician, Vascular Surgical ICU, †† Staff Physician, Polyvalent ICU, Saint Joseph Teaching Hospital. # Staff Physician, Renal ICU, Tenon Teaching Hospital, Paris, France. ** Professor, Medical-surgical ICU, Avicenne Teaching Hospital. ‡‡ Staff Physician, Polyvalent ICU, Delafontaine Hospital, Saint Denis, France. §§ Staff Physician, Surgical ICU, Antoine Béclère Teaching Hospital. ‖‖ Staff Physician, Medical ICU, Bichat-Claude Bernard Teaching Hospital, Paris, France. ## Individuals participating in the OUTCOMEREA Study Group are listed in the Appendix.

Received from the Medical ICU, Avicenne Hospital, Bobigny, France; Surgical ICU, Antoine Béclère Hospital, Clamart, France; Medical and Surgical ICUs, Saint Joseph Hospital, Paris, France; Medical ICU, Louis Mourier Hospital, Colombes, France; and the Medical ICU, Saint-Louis Hospital, Paris, France. Submitted for publication October 22, 2001. Accepted for publication February 27, 2002. OUTCOMEREA® is supported by nonexclusive educational grants from Aventis Pharma France, Paris, France, Wyeth-Lederle, Puteaux-Paris la Défense, France, and Centre National de Recherche Scientifique, Paris, France.

Adress reprint requests to Dr. de Lassence: Service de Réanimation Médicale, Hôpital Louis Mourier, 92701 Colombes Cedex, France. Address electronic mail to: arnaud.de-lassence@outcomerea.org. Individual article reprints may be purchased through the Journal Web site, www.anesthesiology.org.

MECHANICAL ventilation *via* tracheal intubation is widely used in intensive care units (ICUs). Reported complications of mechanical ventilation include nosocomial pneumonia, volutrauma, and barotrauma. Complications related to the endotracheal tube itself[1] consist chiefly of reintubation after weaning and unplanned extubation by the patient (self-extubation) or caregivers (accidental extubation). Unplanned extubation is the most common endotracheal tube accident,[1] accounting for about 10% (3–16%) of extubations and require reintubation in 60% of cases.[2–5] Predisposing factors and prevention have been extensively studied.[3,4,6] Despite the development of predictive indices for weaning or extubation, planned extubation fails in 2–19% of cases.[7–14] In a recent case-control study investigating the impact of unplanned extubation on the outcome of patients receiving mechanical ventilation, Epstein *et al.*[15] found that either form of unplanned extubation was associated with longer times on mechanical ventilation and in the ICU and hospital but not with increased mortality.

Reintubation has been recognized as a leading risk factor for nosocomial pneumonia.[16] The risk of nosocomial pneumonia after reintubation may be associated with factors related to the reintubation procedure itself or to factors related to the previous extubation event. Both the rate of reintubation and the circumstances of prior extubation vary across these three categories. No prospective studies specifically designed to evaluate the impact of each of these categories on the occurrence of nosocomial pneumonia have been published. We conducted a prospective multicenter study to evaluate the impact of reintubation after weaning, of self-extubation, and of accidental extubation on the risk of nosocomial pneumonia.

Patients and Methods

Eligibility Criteria

A prospective study in a multicenter database (OUTCOMEREA®) was conducted during a 2-yr period in six French medical or surgical ICUs. Starting in January 1997, all patients who were older than 16 yr, had an ICU stay length longer than 48 h, and received mechanical ventilation at any time during the ICU stay were entered in the study. Patients who were tracheostomized at ICU admission were excluded from the analyses.

Definitions and Measurements

Method of Data Collection. Data were collected daily by senior physicians in each participating unit. For each patient, an investigator used these data to complete a case report form. All codes and definitions were established prior to study initiation. Before entry into the database, each case report form was reviewed by a member of the steering committee.

Collected Variables. The case report forms contained no information identifying the patient. They were used to record age, sex, and admission category (medical, scheduled surgery, or unscheduled surgery); underlying diseases according to SAPS II definitions[17]; other comorbidities including respiratory, cardiovascular, hepatic, renal, and immunosuppression using APACHE II definitions[18]; and severity of illness at ICU admission and daily during the ICU stay as measured using the SAPS II and LOD system.[19]

All patients were screened daily throughout the ICU stay for suspected nosocomial pneumonia and for self-extubation, accidental extubation, or reintubation after weaning. Self-extubation was defined as deliberate extubation by a patient for whom the intensivists considered that intubation was beneficial, accidental extubation as inadvertent extubation by an ICU caregiver during procedures at the bedside, and reintubation after weaning as a need for reintubation within 48 h after planned extubation. The need for noninvasive mechanical ventilation alone was not considered as an extubation failure.

The sedative regimen used in the overwhelming majority of patients included a combination of a benzodiazepine and an opioid. The level of sedation was routinely titrated to achieve a Ramsay score of 2–3 and was tailored to the needs of each patient depending on the presenting condition.[20,21] In patients with clinical improvement in the initial cause of their respiratory failure, four widely accepted criteria for a trial of extubation were evaluated daily: a ratio of the partial pressure of arterial oxygen over the fraction of inspired oxygen above 200, a positive end-expiratory pressure below 5 cm H_2O, adequate coughing during suctioning, and absence of infusion of sedatives with a Glasgow coma score greater than 14.[22] In addition, in the overwhelming majority of patients subjected to a trial of extubation, the ratio of respiratory frequency over tidal volume was equal to or lower than 105 breaths per minute per liter.[23] Planned extubation was performed only after a successful T-tube trial of 20–30 min.

The sedated Glasgow coma score was defined as the value truly observed, including effect of sedation, and the expected Glasgow coma score was defined as the value of the score expected if the patient was not receiving sedative drugs.

Clinical suspicion of nosocomial pneumonia was based on the criteria described by Andrews *et al.*[24] Nosocomial pneumonia was defined as pneumonia occurring after at least 48 h of mechanical ventilation, according to the recommendations of the First International Consensus Conference on the Clinical Investigation of Ventilator-Associated Pneumonia.[25] The diagnosis of nosocomial pneumonia was based on a chest radiograph showing new pulmonary infiltrates not otherwise explained, positive results of quantitative cultures of a plugged telescopic catheter or protected-specimen brush specimen ($> 10^3$ cfu/ml) or of a bronchoalveolar lavage specimen ($> 10^4$ cfu/ml), and at least two of the following criteria: fever greater than 38°C, purulent bronchial secretions, or peripheral leukocyte count greater than 10,000/mm^3.

Finally, length of mechanical ventilation, length of ICU and hospital stays, and outcomes at ICU and hospital discharges were recorded.

Statistical Analysis

Results were expressed as numerical values and percentages for categorical variables, and as medians and quartiles (25th–75th percentile) for continuous variables. Comparisons were based on the Fisher exact test or chi-square test for categorical data and on paired Wilcoxon tests or Kruskal-Wallis tests for continuous data where appropriate. The relation between iatrogenic events and nosocomial pneumonia was computed using a Cox model with a time-dependent covariate. Time to nosocomial pneumonia was defined as the interval from mechanical ventilation initiation to the first nosocomial pneumonia episode even if nosocomial pneumonia occurred after successful extubation. In patients who had nosocomial pneumonia episodes before and after unplanned extubation and reintubation after weaning ($n = 5$), this time was defined as the interval between mechanical ventilation initiation and the nosocomial pneumonia episode after event. Nosocomial pneumonia episodes that occurred before unplanned extubation or reintubation after weaning were entered into the model as a dichotomous variable. Patients who had no nosocomial pneumonia episodes were censored at ICU discharge. Time to the first self-extubation, accidental extubation, or reintubation after weaning, and time to the first nosocomial pneumonia episode were computed using Kaplan-Meier estimates.

Time to occurrence of the first event (unplanned extubation or reintubation after weaning) and each category of event were successively introduced into the Cox model as time-dependent covariates. In addition, the following variables were studied: SAPS II and LOD on the first mechanical ventilation day, occurrence of pneumonia before mechanical ventilation or within 48 h after mechanical ventilation, enteral feeding, antiacid and antibiotic therapy within 48 h after mechanical ventilation, Knaus comorbidities, main reasons for ICU admission,

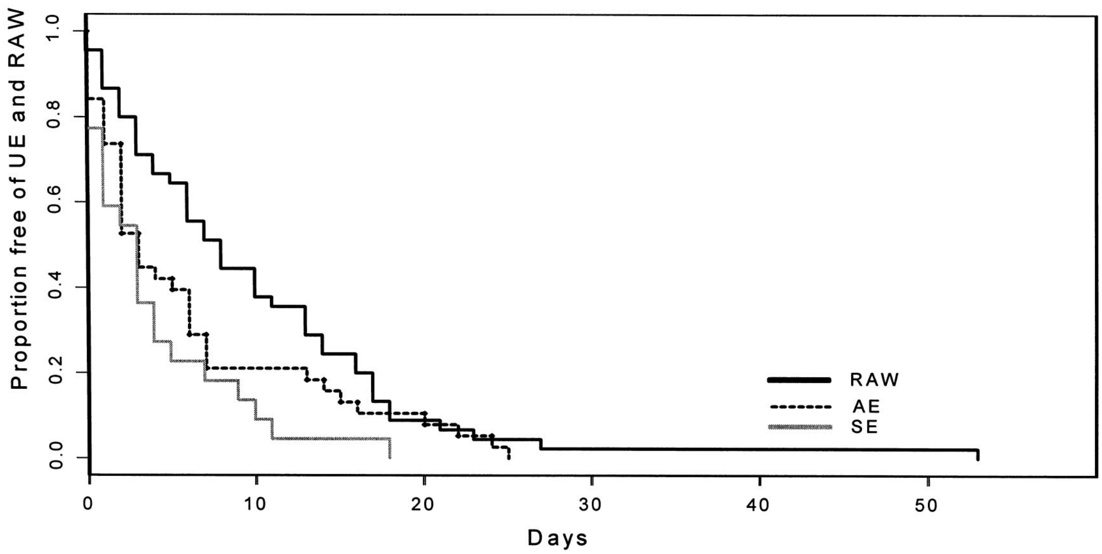

Fig. 1. Time to the first event. RAW = reintubation after weaning; UE = unplanned extubation; AE = accidental extubation; SE = self-extubation.

and whether the patient was transferred to the ICU from a ward. These variables have been reported to affect the risk of mechanical ventilation–related pneumonia.[26] A stepwise forward procedure was used to select variables for entry into the model. Results at the last step are reported.

Factors associated with hospital mortality were evaluated using a Cox model in which unplanned extubation or reintubation after weaning were entered as a time-dependent covariate in addition to the following patient characteristics at ICU admission: SAPS II and LOD, Knaus comorbidities, reasons for ICU admission, and whether the patient was transferred from a ward. Stepwise forward selection was used. At the last step, unplanned extubation and reintubation after weaning were forced into the model to allow an estimation of its effects adjusted on patient characteristics.

All statistical tests were two-tailed, and *P* values less than 5% were considered significant. Statistical tests were performed using the SAS 8.00 (SAS Inc., Cary, NC) and S-plus 2000 (MathSoft Inc., Seattle, WA) software packages for personal computers.

Results

During the 2-yr study period, 1,227 patients were admitted for longer than 48 h to the participating ICUs. During their ICU stay, 750 patients required conventional mechanical ventilation for more than 24 h, including 567 (75.6%) who were ventilated on ICU admission. The median duration of ventilation was 7 days (25th–75th percentile: 3–14 days). Overall, 7,953 patient-ventilation days were investigated, excluding days of ventilation through a tracheostomy and days of noninvasive ventilation.

Of the 750 ventilated patients, 105 (14.0%) experienced 131 events, with 51 self-extubations, 24 accidental extubations, and 56 reintubations after weaning, yielding incidence density rates of 6.4, 3.0, and 7.0 per 1,000 intubation days, respectively. Twenty-three patients experienced more than one category of event. The first event was self-extubation in 38 patients, with a median time to occurrence since mechanical ventilation initiation of 3 days (25th–75th percentile: 2–6); accidental extubation in 22 patients, with a median time of 3 days (25th–75th percentile: 1–4); and reintubation after weaning in 45 patients, with a median time of 8 days (25th–75th percentile: 6–11) (fig. 1).

The 105 patients with unplanned extubation or reintubation after weaning and the 645 patients without unplanned extubation or reintubation after weaning (controls) differed regarding the main causes of ICU admission and the presence of three comorbidities, namely, respiratory, cardiovascular, and immunosuppression (table 1). The SAPS II and LOD scores on the day before events were significantly higher in the accidental extubation group, whereas the P_{O_2}/F_{IO_2} ratio and the sedated Glasgow coma score were significantly lower (table 2).

When we recorded the maximum daily SAPS II and LOD score values during the 2 days preceding and the 3 days following the event, we found a significant increase in these values only in the reintubation after weaning subgroup, in which the maximum daily scores were significantly higher after the event than on the day before the event ($P < 0.01$ and $P = 0.03$ for the SAPS II and LOD, respectively).

Five patients with unplanned extubation or reintubation after weaning (3 planned extubation failure and 2

Table 1. Population Characteristics on ICU Admission

Median (25th–75th Percentile) [n (%)]	MV Population (n = 750)	Control (n = 645)	RAW + UE (n = 105)	*P* Value
Age	67 (54–75)	67 (53–75)	70 (56–76)	0.21
Sex (male)	478 (63.7)	408 (63.3)	70 (66.7)	0.7
Main reason for admission				0.01
Coma	137 (18.3)	113 (17.5)	24 (22.9)	
Acute respiratory failure	226 (30.1)	189 (29.3)	37 (35.2)	
Shock	173 (23.1)	154 (23.9)	19 (18.1)	
MOF	48 (6.4)	42 (6.5)	6 (5.7)	
Trauma	11 (1.5)	10 (1.5)	1 (1.0)	
COPD	52 (6.9)	39 (6.0)	13 (12.4)	
Other	103 (13.7)	98 (15.2)	5 (4.8)	
Admission category				0.55
Medical	464 (61.9)	394 (61.1)	70 (66.7)	
Scheduled surgery	97 (12.9)	85 (13.2)	12 (11.4)	
Unscheduled surgery	189 (25.2)	166 (25.7)	23 (21.9)	
Chronic disease				
None	406 (54.1)	356 (54.9)	50 (49.0)	
Respiratory	146 (19.5)	118 (18.3)	28 (26.7)	0.04
Cardiovascular	87 (11.6)	65 (10.1)	22 (21.0)	0.001
Hepatic	52 (6.9)	49 (7.6)	3 (2.9)	0.08
Renal	11 (1.5)	10 (1.5)	1 (1.0)	0.63
Immunosuppression	107 (14.3)	99 (15.3)	8 (7.6)	0.04
SAPS II	47 (35–58)	46 (35–58)	49 (37–58)	0.26
MV on admission	567 (75.6)	484 (75.0)	83 (79.0)	0.37

ICU = intensive care unit; MV = mechanical ventilation; RAW = reintubation after weaning; UE = unplanned extubation; MOF = multiple organ failure; COPD = chronic obstructive pulmonary disease; SAPS = Simplified Acute Physiologic Score.

self-extubations) were treated with noninvasive mechanical ventilation.

Complications of Undesirable Extubation

Reintubation within 48 h after the event was required in all accidental extubations but in only 24 of 38 (63.2%) self-extubations. Among the 91 patients who underwent reintubation, including reintubation after weaning, six (5.7%) were tracheostomized within 48 h after event (reintubation after weaning: 1; accidental extubation: 1; and self-extubation: 4).

Among the 750 patients, 125 (16.7%) acquired 163 episodes of nosocomial pneumonia (table 3). The crude incidence of nosocomial pneumonia was significantly higher in the patients with unplanned extubation or reintubation after weaning (36 of 105; 34.3%) than in the controls (89 of 645; 13.8%) ($P < 0.01$). This significant difference persisted after exclusion of nosocomial pneumonia episodes that preceded the first event (29 of 105; 27.6%; $P = 0.0003$).

Nosocomial pneumonia after event was significantly more common in the accidental extubation subgroup (11 of 22; 50%) than in the reintubation after weaning subgroup (11 of 45; 24.4%) and self-extubation subgroup (7 of 38, 18.4%) ($P = 0.02$). When introduced in a Cox model as a time-dependent covariate, unplanned extubation and reintubation after weaning increased the risk of nosocomial pneumonia (relative risk, 1.80; 95% confidence interval, 1.15–2.80; $P = 0.009$) even after adjustment on SAPS II and LOD on the first mechanical ventilation day, enteral feeding, gastric protection by antihistamine type 2 receptors and proton pump inhibitors, and antimicrobial therapy within 48 h after mechanical ventilation initiation (table 4, which shows only significant variables).

When we studied these three categories of events separately, we found that the increase in nosocomial pneumonia risk associated with unplanned extubation and reintubation after weaning was entirely attributable

Table 2. Severity and Underlying Conditions 24 h before the First Event

Events	RAW + UE (n = 105)	RAW (n = 45)	AE (n = 22)	SE (n = 38)	*P* Value
SAPS II	39 (32–48)	39 (31–49)	48 (38–57)	38 (32–44)	0.027
LOD score	4 (2–6)	4 (2–6)	7 (5–7)	4 (2–6)	0.008
Expected Glasgow Coma Score	15 (13–15)	15 (14–15)	14 (6–15)	14 (12–15)	0.04
Sedated Glasgow Coma Score	13 (7–15)	15 (13–15)	6 (3–13)	12 (7–15)	$< 10^{-3}$
Pa_{O_2}/F_{IO_2} ratio	273 (212–363)	314 (247–367)	228 (192–316)	278 (222–360)	0.05
Oral intubation	95 (90.5)	43 (95.6)	18 (81.8)	34 (89.5)	0.16

RAW = reintubation after weaning; UE = unplanned extubation; AE = accidental extubation; SE = self-extubation; SAPS = Simplified Acute Physiologic Score; LOD = logistic organ dysfunction; Pa_{O_2} = arterial oxygen tension; F_{IO_2} = fraction of inspired oxygen.

Table 3. Risk Factors for Nosocomial Pneumonia Occurring after the Beginning of Mechanical Ventilation

Variables	RR	95% CI	*P* Value	RR	95% CI	*P* Value
All events (RAW + UE)	1.80	1.15–2.80	0.009			
AE				5.28	2.83–9.89	$< 10^{-3}$
SAPS II at MV	0.99	0.98–1.00	0.044	0.99	0.97–1.00	0.03
Enteral feeding at MV	1.77	1.23–2.53	0.002	1.85	1.30–2.65	0.0007

RR = risk ratio; CI = confidence interval; RAW = reintubation after weaning; UE = unplanned extubation; AE = accidental extubation; SAPS = Simplified Acute Physiologic Score; MV = mechanical ventilation.

to an association with accidental extubation (relative risk, 5.28; 95% confidence interval, 2.83–9.89; $P < 0.01$; table 3). Conversely, no associations with nosocomial pneumonia were found for reintubation after self-extubation (relative risk, 1.83; 95% confidence interval, 0.85–3.96; $P = 0.12$) or reintubation after weaning (relative risk, 1.35; 95% confidence interval, 0.7–2.61; $P = 0.36$). Figure 2 shows that accidental extubations are at earlier risk of nosocomial pneumonia and that the proportion of patients with nosocomial pneumonia is higher with accidental extubations.

Hospital Outcomes of Undesirable Extubation

Total mechanical ventilation duration was significantly longer in the unplanned extubation and reintubation after weaning groups (median, 17 days; 25th–75th percentile: 8–24) than in the control group (median, 6 days; 25th–75th percentile: 3–12) ($P < 0.01$). Significant differences in the same direction were found for ICU and hospital length of stay (table 4). Moreover, mechanical ventilation duration was significantly higher in the subgroup with reintubation after weaning than in the other two subgroups. Tracheostomy was performed in a larger proportion of patients with unplanned extubation or reintubation after weaning (22.9%; reintubation after weaning: 13; accidental extubation: 5; and self-extubation: 6) than of controls (6.0%; n = 39) ($P < 0.01$). The overall additional mechanical ventilation durations after the first event were 11 days (range, 7–16 days), 7 days (range, 5–13 days), and 4 days (range, 1–13 days) for reintubation after weaning, accidental extubation, and self-extubation, respectively.

Unplanned extubation or reintubation after weaning did not influence ICU or hospital mortality rates (table 4), even after adjustment on SAPS II at ICU admission, comorbidities, and reasons for ICU admission.

Discussion

Self-extubation, accidental extubation, and reintubation after weaning are common in the ICU. These three categories of events put patients at significant risk of morbidity and can contribute to death.[5] Although unplanned extubation or reintubation after weaning have been extensively investigated since 1990, most studies focused on incidence, risk factors, prevention, and prediction of early reintubation. Data on adverse events, including nosocomial pneumonia, are sparse. Adverse event rates after unplanned extubation have ranged from 5% to 28%,[27] and life-threatening complications have been reported. All studies of the outcome of unplanned extubation used a retrospective case-control design.[7,8,15,16] We report the first large, prospective, multicenter study evaluating the occurrence and outcomes of all three categories of events, with the primary objective of looking for nosocomial pneumonia rate differences possibly related to differences in reintubation rates or to differences in the circumstances surrounding extubation.

Table 4. Duration of Mechanical Ventilation, Length of Stay, and Mortality Rate among 750 Mechanically Ventilated Patients

Median (Q1–Q2) [n (%)]	All (n = 750)	Control Group (n = 645)	RAW + UE (n = 105)	*P* Value	RAW (n = 45)	AE (n = 22)	SE (n = 38)	*P* Value
Ventilation								
Duration of MV	7 (3–14)	6 (3–12)	17 (8–24)	< 0.001	21 (14–28)	12 (7–19)	13 (5–21)	0.005
Cumulated MV days	7,953	6,020	1,933		1,021	345	567	
Duration of MV before event	—	—	5 (3–12)		9 (4–15)	4 (2–6)	4 (2–8)	
Duration of MV after event	—	—	8 (4–15)		11 (7–16)	7 (5–13)	4 (1–13)	
Mortality								
ICU mortality rate	276 (36.8)	245 (38.0)	31 (29.5)	0.10	14 (31.1)	9 (40.9)	8 (21.1)	0.25
Hospital mortality rate	329 (43.9)	286 (44.3)	43 (41.0)	0.52	20 (44.4)	12 (54.5)	11 (29.0)	0.12
LOS								
ICU LOS (days)	10 (6–20)	9 (5–17)	22 (11–40)	< 0.001	27 (18–43)	19 (9–35)	18 (10–36)	0.04
ICU LOS before event	—	—	6 (3–14)		9 (4–16)	4 (4–6)	6 (3–8)	
ICU LOS after event	—	—	15 (8–27)		16 (10–29)	11 (7–34)	14 (6–24)	
Hospital LOS (days)	21 (10–37)	18 (9–33)	34 (22–54)	< 0.001	38 (25–68)	31 (16–45)	30 (18–49)	0.11

RAW = reintubation after weaning; UE = unplanned extubation; AE = accidental extubation; SE = self-extubation; MV = mechanical ventilation; ICU = intensive care unit; LOS = length of stay.

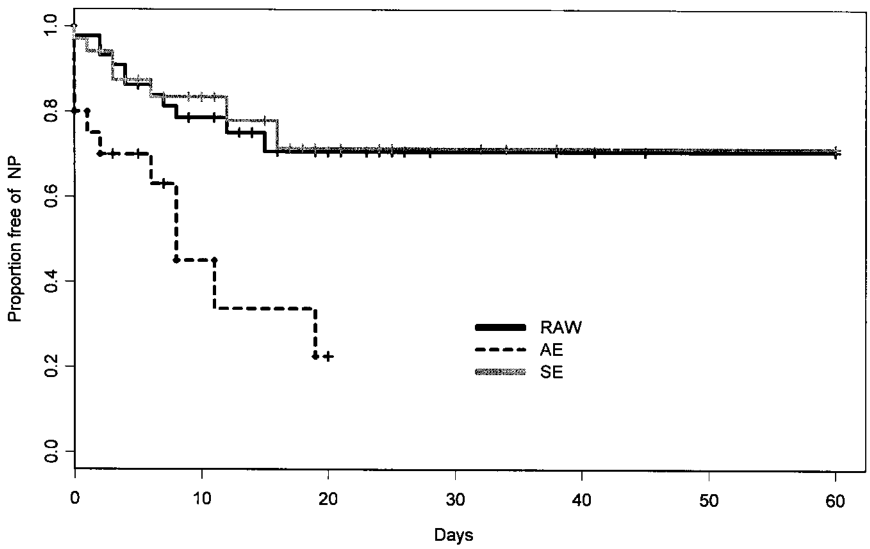

Fig. 2. Time to occurrence of the first nosocomial pneumonia episode in each of the three categories (time to first nosocomial pneumonia was computed from day of event to nosocomial pneumonia occurring after event). NP = nosocomial pneumonia; RAW = reintubation after weaning; AE = accidental extubation; SE = self-extubation.

The limitations of this study need to be discussed. First, the use of continuous intravenous sedation is associated with the prolongation of mechanical ventilation and a greater incidence of reintubation, and could be a risk factor for nosocomial pneumonia.[28] We did not use daily interruption of sedative drug infusion as suggested by Kress *et al.*,[29] since the results of their study had not been published at the time the data on our patients were collected. Sedative drug interruption may influence the rate of unplanned extubation. Second, the ICU patients in the present study were all hospitalized for longer than 48 h. Consequently, the self-extubation subgroup was not representative of the overall population with this event, which often occurs shortly after ICU admission of suicidal or postsurgical patients. This probably led us to underestimate the proportion of self-extubated patients who did not require reintubation. Third, among patients with unplanned extubation, those with accidental extubation were significantly more likely to require reintubation than those with self-extubation.[4] The rate of accidental extubation was higher in our unplanned extubation group (37%) than in other series (0–22%).[2–6,15,27,30] This explains why the overall reintubation rate among patients with unplanned extubation (77%) was at the upper end of the range reported in the literature (30–88%).[2–4,6,15,27,30,31] Fourth, the Consensus Conference criteria from 1993 that we used for diagnosis of ventilatory associated pneumonia could be viewed as out-of-date. However, all patients were similarly screened for diagnosis of nosocomial pneumonia.

In our population, incidence rates were 4.8% for self-extubation and 2.8% for accidental extubation (7.6% for unplanned extubation). These rates are similar to the 3–16% rates of self-extubation found in other studies.[3,4,6,15,30,32–35] Our incidence rate of reintubation after weaning was 6%, which is within the 2–19% range reported in the literature.[7–14,22] This wide range reflects differences in the time to reintubation used to define reintubation after weaning (from within 24 h to within 72 h of planned extubation).

Recent studies have measured the frequency of unplanned extubation as incidence densities. Values ranged from 1.6 to 40 per 1,000 mechanical ventilation days, which is in agreement with our value of 9.4.[1,2,15,31,35–37]

In agreement with most previous studies, we found no increase in mortality in the patients who experienced unplanned extubation or reintubation after weaning, as compared with the controls.[3,15,27,30,33,38,39] The recent literature found that reintubation was associated with an increase in mortality rate.[4,7,11,31] In the present study, the mortality rate was nonsignificantly higher in the patients with accidental extubation or reintubation after weaning, all of whom required reintubation. Several recent series found that mortality was significantly higher in patients with reintubation after weaning,[7,8,10,11] ranging from 32% to 43%, in keeping with our findings; mortality was only 4–12% in successfully extubated patients.[7,8,10,11,16]

Our study hypothesis was that the rate of nosocomial pneumonia would vary across these three categories as a result of differences in reintubation rates or in the circumstances surrounding the previous extubation. Reintubation can introduce colonized oropharyngeal secretions into the lower airways.[40] Torres *et al.*[16] reported that reintubation was among the most significant risk factors for nosocomial pneumonia, with a sixfold risk increase. However, these studies failed to distinguish between the risk of nosocomial pneumonia associated with reintubation *per se* and the risk associated with the circumstances of extubation. Our findings support a role for these circumstances: although we found nosocomial pneumonia rate differences across categories, those differences did not mirror reintubation rates. The reintubation rate was far lower in the self-extubation category, and the rate of nosocomial pneumonia was also lower in these patients. However, all patients with reintubation after weaning or accidental extubation required reintubation, but nosocomial pneumonia was far more common in the accidental extubation category. Several factors may explain these differences. The pathogenesis of nosocomial pneumonia is related to aspiration of pharyngeal contents or gastric content[41] into the distal airways. Factors that may affect the risk of nosocomial pneumonia after unplanned extubation or reintubation after weaning include altered glottic function after several days of intubation, trauma related to the inflated tube cuff in unplanned extubation, prior level of sedation, level of consciousness after extubation,[42] presence of a nasogastric tube during the extubation period,[43] body position, and time spent extubated.[16] Reintubation after weaning occurred when the patients were awake, whereas in our accidental extubation subgroup alterations in consciousness were present in most patients (median sedated Glasgow coma score, 6) and the median Pa_{O_2}/F_{IO_2} ratio was significantly lower than in the other two groups. Both parameters have been found to be associated with reintubation.[4] Although by definition reintubation is always performed after reintubation after weaning, removal of the tube in this situation is done under optimal conditions, including stomach emptying, previous cessation of enteral feeding, careful airways suctioning, deflation of the tube cuff, and close monitoring. Most studies of nosocomial pneumonia rates in patients with unplanned extubation[7,8,10,11,16] found no significant association[3,5,7,27] but included few[7,27] or no[3,5] patients with accidental extubation. Accidental extubations may occur in sicker patients with heavier workload and therefore more opportunities of manipulations leading to accidental events. However, in the Cox model we used, adjustment on severity and organ failure scores has been performed. Therefore, this study shows clearly that accidental extubation remains an independent predictor of nosocomial pneumonia, adjusted on patients severity.

Total mechanical ventilation duration was significantly longer in our self-extubation, accidental extubation, and reintubation after weaning subgroups than in the controls, and all three events were significantly associated with longer ICU and hospital stays. Moreover, although the self-extubated patients were less likely to undergo reintubation, their mechanical ventilation length, ICU stay length, and hospital stay length were significantly longer than in the controls. In keeping with our findings, Epstein *et al.*[7] reported than mechanical ventilation duration was about 2 weeks longer in patients who underwent reintubation. In contrast, in a case-control study by Chevron and coworkers,[4] total mechanical ventilation length was significantly lower in patients with than without unplanned extubation (9 days and 16 days, respectively). This discrepancy may be ascribable in part to the low reintubation rate (37%) in the study by Chevron *et al.*[4] and in part to exclusion from our study of patients with ICU stays shorter than 48 h. Nevertheless, it has been suggested that unplanned extubation not followed by reintubation indicates that planned extubation was overdue and that this may translate into a higher rate of ventilator-related complications, a longer ICU stay, and higher costs.[34]

Given that unplanned extubation and reintubation after weaning were associated with longer durations of mechanical ventilation and hospital stay, these events are markers for suboptimal quality of care. Both reintubation after weaning (with its risk of health status deterioration) and accidental extubation (with its risk of nosocomial pneumonia) can be reduced by improving the quality of care. Self-extubation is also partly preventable.[1] Initiation of a continuous quality improvement program was followed by a decrease in the self-extubation rate from 2.6% to 1.2% per patient-ventilator day.[36] It has been suggested that unplanned extubation should be viewed as quality-control issues.[44] These events correspond to different facets of suboptimal care. Accidental extubation may be related to less-than-ideal nursing care. In a recent study, accidental extubation was the fourth most common incident observed in ICUs with nurse understaffing.[45] In a study that used the PRN_{REA} score, Chevron *et al.*[4] demonstrated that accidental extubation was not related to the nurse workload, suggesting that this event may be a consequence of faulty nursing care and could be used as an indicator for nursing care quality. Self-extubation without subsequent reintubation may indicate that intubation was maintained too long because the intensivists underestimated the patient's ability to tolerate weaning; reintubation after weaning may reflect overestimation of this ability. Attempts to prevent self-extubation may result either in premature planned extubation responsible for an increase in the rate of reintubation after weaning or in increased use of deep sedation responsible for an increase in mechanical ventilation duration.[46] In both cases, mechanical ventilation duration would be increased. Whether clinical judgment used alone or in combination with mechanical respiratory indices, such as frequency/tidal volume, is effective in predicting successful extubation remains controversial.[10,12–14,23,47] Continuous quality control programs should evaluate clinical procedures, including clinical indicators, predictive weaning indexes based on pulmonary function parameters, and daily routine evaluation of criteria for a trial of extubation, the goal being to extubate patients as soon as possible but not too soon.[13,14,22,29,47] It would be of interest to evaluate both self-extubation and reintubation after weaning as part of a continuous quality improvement program to determine the ratio of self-extubation over reintubation after weaning that minimizes ventilator days, length of stay, and mechanical ventilation–related complications. To be relevant, a quality indicator should be a common event that is associated with morbidity, easy to detect prospectively, and amenable to prevention.[48] Unplanned extubation and reintubation after weaning meet all of these requirements and consequently deserve evaluation as quality indicator for quality improvement programs.

References

1. Kapadia FN, Bajan KB, Raje KV: Airway accidents in intubated intensive care unit patients: An epidemiological study. Crit Care Med 2000; 28:659–64
2. Christie JM, Dethlefsen M, Cane RD: Unplanned endotracheal extubation in the intensive care unit. J Clin Anesth 1996; 8:289–93
3. Boulain T: Unplanned extubations in the adult intensive care unit: A prospective multicenter study. Association des Reanimateurs du Centre-Ouest. Am J Respir Crit Care Med 1998; 157:1131–7
4. Chevron V, Menard JF, Richard JC, Girault C, Leroy J, Bonmarchand G: Unplanned extubation: Risk factors of development and predictive criteria for reintubation. Crit Care Med 1998; 26:1049–53
5. Mort TC: Unplanned tracheal extubation outside the operating room: A quality improvement audit of hemodynamic and tracheal airway complications associated with emergency tracheal reintubation. Anesth Analg 1998; 86:1171–6
6. Vassal T, Anh NG, Gabillet JM, Guidet B, Staikowsky F, Offenstadt G: Prospective evaluation of self-extubations in a medical intensive care unit. Intensive Care Med 1993; 19:340–2
7. Epstein SK, Ciubotaru RL, Wong JB: Effect of failed extubation on the outcome of mechanical ventilation. Chest 1997; 112:186–92
8. Daley BJ, Garcia-Perez F, Ross SE: Reintubation as an outcome predictor in trauma patients. Chest 1996; 110:1577–80
9. Brochard L, Rauss A, Benito S, Conti G, Mancebo J, Rekik N, Gasparetto A, Lemaire F: Comparison of three methods of gradual withdrawal from ventilatory support during weaning from mechanical ventilation. Am J Respir Crit Care Med 1994; 150:896–903
10. Esteban A, Alia I, Tobin MJ, Gil A, Gordo F, Vallverdu I, Blanch L, Bonet A, Vazquez A, de Pablo R, Torres A, de La Cal MA, Macias S: Effect of spontaneous breathing trial duration on outcome of attempts to discontinue mechanical ventilation. Spanish Lung Failure Collaborative Group. Am J Respir Crit Care Med 1999; 159:512–8
11. Esteban A, Alia I, Gordo F, Fernandez R, Solsona JF, Vallverdu I, Macias S, Allegue JM, Blanco J, Carriedo D, Leon M, de la Cal MA, Taboada F, Gonzalez de Velasco J, Palazon E, Carrizosa F, Tomas R, Suarez J, Goldwasser RS: Extubation outcome after spontaneous breathing trials with T-tube or pressure support ventilation. The Spanish Lung Failure Collaborative Group. Am J Respir Crit Care Med 1997; 156:459–65
12. Lee KH, Hui KP, Chan TB, Tan WC, Lim TK: Rapid shallow breathing (frequency-tidal volume ratio) did not predict extubation outcome. Chest 1994; 105:540–3
13. Leitch EA, Moran JL, Grealy B: Weaning and extubation in the intensive care unit: Clinical or index-driven approach? Intensive Care Med 1996; 22:752–9
14. Namen AM, Ely EW, Tatter SB, Case LD, Lucia MA, Smith A, Landry S, Wilson JA, Glazier SS, Branch CL, Kelly DL, Bowton DL, Haponik EF: Predictors of successful extubation in neurosurgical patients. Am J Respir Crit Care Med 2001; 163:658–64
15. Epstein SK, Nevins ML, Chung J: Effect of unplanned extubation on outcome of mechanical ventilation. Am J Respir Crit Care Med 2000; 161:1912–6
16. Torres A, Gatell JM, Aznar E, El-Ebiary M, Puig de la Bellacasa J, Gonzalez J, Ferrer M, Rodriguez-Roisin R: Re-intubation increases the risk of nosocomial pneumonia in patients needing mechanical ventilation. Am J Respir Crit Care Med 1995; 152:137–41
17. Le Gall JR, Lemeshow S, Saulnier F: A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. JAMA 1993; 270:2957–63
18. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: A severity of disease classification system. Crit Care Med 1985; 13:818–29
19. Le Gall JR, Klar J, Lemeshow S, Saulnier F, Alberti C, Artigas A, Teres D: The Logistic Organ Dysfunction system: A new way to assess organ dysfunction in the intensive care unit. ICU Scoring Group. JAMA 1996; 276:802–10
20. XI°conference de consensus en réanimation et médecine d'urgence. Sédation en réanimation. Réanim Urg 1993; 2:437–517
21. Ramsay MA, Savege TM, Simpson BR, Goodwin R: Controlled sedation with alphaxalone-alphadolone. BMJ 1974; 2:656–9
22. Ely EW, Baker AM, Dunagan DP, Burke HL, Smith AC, Kelly PT, Johnson MM, Browder RW, Bowton DL, Haponik EF: Effect on the duration of mechanical ventilation of identifying patients capable of breathing spontaneously. N Engl J Med 1996; 335:1864–9
23. Yang KL, Tobin MJ: A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. N Engl J Med 1991; 324:1445–50
24. Andrews CP, Coalson JJ, Smith JD, Johanson WG Jr: Diagnosis of nosocomial bacterial pneumonia in acute, diffuse lung injury. Chest 1981; 80:254–8
25. Wunderink RG MC, Gibert C: Methodology for clinical investigation of ventilator associated pneumonia: Epidemiology and therapeutic interventions. Chest 1993; 102:580S–8S
26. Cook DJ, Walter SD, Cook RJ, Griffith LE, Guyatt GH, Leasa D, Jaeschke RZ, Brun-Buisson C: Incidence of and risk factors for ventilator-associated pneumonia in critically ill patients. Ann Intern Med 1998; 129:433–40
27. Atkins PM, Mion LC, Mendelson W, Palmer RM, Slomka J, Franko T: Characteristics and outcomes of patients who self-extubate from ventilatory support: A case-control study. Chest 1997; 112:1317–23
28. Kollef MH, Levy NT, Ahrens TS, Schaiff R, Prentice D, Sherman G: The use of continuous i.v. sedation is associated with prolongation of mechanical ventilation. Chest 1998; 114:541–8
29. Kress JP, Pohlman AS, O'Connor MF, Hall JB: Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. N Engl J Med 2000; 342:1471–7
30. Betbese AJ, Perez M, Bak E, Rialp G, Mancebo J: A prospective study of unplanned endotracheal extubation in intensive care unit patients. Crit Care Med 1998; 26:1180–6
31. Carrion MI, Ayuso D, Marcos M, Paz Robles M, de la Cal MA, Alia I, Esteban A: Accidental removal of endotracheal and nasogastric tubes and intravascular catheters. Crit Care Med 2000; 28:63–6
32. Tindol GA Jr, DiBenedetto RJ, Kosciuk L: Unplanned extubations. Chest 1994; 105:1804–7
33. Coppolo DP, May JJ: Self-extubations: A 12-month experience. Chest 1990; 98:165–9
34. Razek T, Gracias V, Sullivan D, Braxton C, Gandhi R, Gupta R, Malcynski J, Anderson HL, Reilly PM, Schwab CW: Assessing the need for reintubation: A prospective evaluation of unplanned endotracheal extubation. J Trauma 2000; 48:466–9
35. Kapadia FN, Bajan KB, Singh S, Mathew B, Nath A, Wadkar S: Changing patterns of airway accidents in intubated ICU patients. Intensive Care Med 2001; 27:296–300
36. Chiang AA, Lee KC, Lee JC, Wei CH: Effectiveness of a continuous quality improvement program aiming to reduce unplanned extubation: A prospective study. Intensive Care Med 1996; 22:1269–71
37. Tominaga GT, Rudzwick H, Scannell G, Waxman K: Decreasing unplanned extubations in the surgical intensive care unit. Am J Surg 1995; 170:586–9; discussion 589–90
38. Listello D, Sessler CN: Unplanned extubation: Clinical predictors for reintubation. Chest 1994; 105:1496–503
39. Zwillich CW, Pierson DJ, Creagh CE, Sutton FD, Schatz E, Petty TL: Complications of assisted ventilation: A prospective study of 354 consecutive episodes. Am J Med 1974; 57:161–70
40. Torres A, Aznar R, Gatell JM, Jimenez P, Gonzalez J, Ferrer A, Celis R, Rodriguez-Roisin R: Incidence, risk, and prognosis factors of nosocomial pneumonia in mechanically ventilated patients. Am Rev Respir Dis 1990; 142:523–8
41. Torres A, el-Ebiary M, Gonzalez J, Ferrer M, Puig de la Bellacasa J, Gene A, Martos A, Rodriguez-Roisin R: Gastric and pharyngeal flora in nosocomial pneumonia acquired during mechanical ventilation. Am Rev Respir Dis 1993; 148: 352–7
42. Chevret S, Hemmer M, Carlet J, Langer M: Incidence and risk factors of pneumonia acquired in intensive care units: Results from a multicenter prospective study on 996 patients. European Cooperative Group on Nosocomial Pneumonia. Intensive Care Med 1993; 19:256–64
43. Ibanez J, Penafiel A, Raurich JM, Marse P, Jorda R, Mata F: Gastroesophageal reflux in intubated patients receiving enteral nutrition: Effect of supine and semirecumbent positions. J Parenter Enteral Nutr 1992; 16:419–22
44. Sessler CN: Unplanned extubations: Making progress using CQI. Intensive Care Med 1997; 23:143–5
45. Beckmann U, Baldwin I, Durie M, Morrison A, Shaw L: Problems associated with nursing staff shortage: An analysis of the first 3600 incident reports submitted to the Australian Incident Monitoring Study (AIMS-ICU). Anaesth Intensive Care 1998; 26:396–400
46. Kapadia F: Effect of unplanned extubation on outcome of mechanical ventilation. Am J Respir Crit Care Med 2001; 163:1755–6
47. Epstein SK: Etiology of extubation failure and the predictive value of the rapid shallow breathing index. Am J Respir Crit Care Med 1995; 152:545–9
48. An approach to the evaluation of quality indicators of the outcome of care in hospitalized patients, with a focus on nosocomial infection indicators. The Quality Indicator Study Group. Infect Control Hosp Epidemiol 1995; 16:308–16

Appendix

The following is the list of people who belong to the OUTCOMEREA® Study Group, including all authors of the present manuscript. Scientific committee: Jean-François Timsit, M.D., Staff Physician, ICU, Hôpital Bichat, Paris, France; Pierre Moine, M.D., Ph.D., Staff Physician, DAR, Hôpital Lariboisiere, Paris, France; Arnaud de Lassence, M.D., Staff Physician, ICU, Hôpital Louis Mourier, Colombes, France; Élie Azoulay, M.D., Staff Physician, ICU, Hôpital Saint Louis, Paris, France; Yves Cohen, M.D., Professor, ICU, Hôpital Avicenne, Bobigny, France;

Maïté Garrouste-Orgeas, M.D., Staff Physician, ICU, Hôpital Saint Joseph, Paris, France; Jean-Philippe Fosse, M.D., Staff Physician, ICU, Hôpital Avicenne, Bobigny, France; Lilia Soufir, M.D., Staff Physician, ICU, Hôpital des Diaconesses, Paris, France; Jean-Ralph Zahar, M.D., Staff Physician, Infectious Diseases Deparment, CH François Quesnay, Mantes la Jolie, France; Christophe Adrie, M.D., Staff Physician, ICU, Hôpital de la Fontaine, Saint Denis, France; Gilles Troché, M.D., Staff Physician, Hôpital A. Beclere, Clamart, France; Jean Carlet, M.D., Staff Physician, ICU, Hôpital Saint Joseph, Paris, France; François L'Heriteau, M.D., Attending Physician, ICU, Hôpital Bichat, Paris, France. Biostatistical and informatical expertise: Sylvie Chevret, Ph.D., Professor, DBIM, Hôpital Saint Louis, Paris, France; Corinne Alberti, M.D., Staff Physician, DBIM, Hôpital Saint Louis, Paris, France; Frederik Lecorre, Informatician, Supelec, France. Investigators of the OutcomeRea Data Base: Caroline Bornstain, M.D., Staff Physician, ICU, HEGP, Paris, France; Marie Thuong, M.D., Staff Physician, ICU, Hôpital de la Fontaine, Saint Denis, France; Marie-Alliette Costa de Beauregard, M.D., Staff Physician, Nephrology, Hôpital Tenon, Paris, France; Jean-Pierre Colin, M.D., Staff Physician, ICU, CH de Dourdan, Dourdan, France; Eric Le Miere, M.D., Attending Physician, ICU, Hôpital Louis Mourier, Colombes, France; Caubel Antoine, M.D., Attending Physician, ICU, Hôpital Saint Joseph, Paris, France; Christine Cheval, M.D., Staff Physician, SICU, Hôpital Saint Joseph, Paris, France; Eric Vatalon, M.D., Staff Physician, SICU, Hôpital Saint Joseph, Paris, France; François Vincent, M.D., Staff Physician, Nephrology, Hôpital Tenon, Paris, France; Amar Salah, M.D., Staff Physician, ICU, Hôpital Louis Mourier, Colombes, France; Laurent Montessino, M.D., Attending Physician, ICU, Hôpital Bichat, Paris, France; Etienne Pigné, M.D., Staff Physician, ICU, Hôpital Louis Mourier, Colombes, France; Alexandre Boyer, M.D., Staff Physician, ICU, Hôpital Pellegrin, Bordeaux, France; Olivier Tuill, M.D., Staff Physician, ICU, Hôpital Avicenne, Bobigny, France; Bruno Mourvillier, M.D., Staff Physician, ICU, Hôpital Bichat, Paris, France; Samir Jamali, M.D., Staff Physician, ICU, CH de Dourdan, Dourdan, France; Delphine Moreau, M.D., Staff Physician, ICU, Hôpital Saint Louis, Paris, France; Guillaume Thiery, M.D., Staff Physician, ICU, Hôpital Saint Louis, Paris, France; Alexandre Duguet, M.D., Attending Physician, Hôpital Pitié-Salpetriere, Paris, France; Christian Laplace, M.D., Attending Physician, ICU, Hôpital Kremlin-Bicetre, Bicetre, France.