Intensive Care Med (2017) 43:1793–1807
DOI 10.1007/s00134-017-4891-0

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Terminal weaning or immediate extubation for withdrawing mechanical ventilation in critically ill patients (the ARREVE observational study)

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Abstract

Purpose: The relative merits of immediate extubation versus terminal weaning for mechanical ventilation withdrawal are controversial, particularly regarding the experience of patients and relatives.

Methods: This prospective observational multicentre study (ARREVE) was done in 43 French ICUs to compare terminal weaning and immediate extubation, as chosen by the ICU team. Terminal weaning was a gradual decrease in the amount of ventilatory assistance and immediate extubation was extubation without any previous decrease in ventilatory assistance. The primary outcome was posttraumatic stress symptoms (Impact of Event Scale Revised, IES-R) in relatives 3 months after the death. Secondary outcomes were complicated grief, anxiety, and depression symptoms in relatives; comfort of patients during the dying process; and job strain in staff.

Results: We enrolled 212 (85.5%) relatives of 248 patients with terminal weaning and 190 relatives (90.5%) of 210 patients with immediate extubation. Immediate extubation was associated with airway obstruction and a higher

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Take-home message: Using immediate extubation or terminal weaning to withdraw mechanical ventilation was not associated with additional psychological distress in relatives when each method was standard practice in the ICU where it was applied, in the ARREVE multicentre observational study. However, worse patient discomfort with immediate extubation compared to terminal weaning indicated room for improving end-of-life care.

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mean Behavioural Pain Scale score compared to terminal weaning. In relatives, IES-R scores after 3 months were not significantly different between groups (31.9 ± 18.1 versus 30.5 ± 16.2, respectively; adjusted difference, −1.9; 95% confidence interval, −5.9 to 2.1; $p = 0.36$); neither were there any differences in complicated grief, anxiety, or depression scores. Assistant nurses had lower job strain scores in the immediate extubation group.

Conclusions: Compared to terminal weaning, immediate extubation was not associated with differences in psychological welfare of relatives when each method constituted standard practice in the ICU where it was applied. Patients had more airway obstruction and gasps with immediate extubation.

Trial registration: ClinicalTrials.gov identifier: NCT01818895.

Keywords: Critical care, Treatment limitation, Terminal weaning, Immediate extubation, Mechanical ventilation, Ethics

Introduction

Worldwide, an increasing number of deaths occur in the intensive care unit (ICU) after a decision to withdraw life support [1–5]. A major goal is to avoid unnecessary suffering due to prolongation of the dying process. Relatives of patients who die in the ICU have been reported to experience psychological distress manifesting as post-traumatic stress syndrome (PTSD)-related symptoms, complicated grief, anxiety, and/or depression, to degrees that vary according to the treatments provided and the quality of dying of the patient [6–8].

Withdrawal of mechanical ventilation holds a special place in the process of discontinuing life-sustaining treatments in ICU patients. Mechanical ventilation is withdrawn either by immediate extubation or by terminal weaning (gradual decrease in ventilatory support). The choice between these two methods is controversial, and whether it influences the experience of the patients and relatives is unclear [9–11]. The main challenge to mechanical ventilation withdrawal consists in preventing discomfort to the patient and, therefore, additional distress in the relatives [12–14]. In addition, mechanical ventilation has a deep psychological meaning, as it maintains breathing, which symbolizes life in many cultures. Compared to terminal weaning, immediate extubation is generally viewed as providing a more natural dying process, with less ambiguity, but with a higher risk of patient discomfort related to airway obstruction [14]. Previous studies suggested better satisfaction and lower rates of complicated grief among relatives of patients who died without the endotracheal tube [15, 16]. Other data, however, suggest greater family satisfaction after terminal weaning and worse patient distress after immediate extubation [15, 17]. No study has compared the psychological variables of relatives after terminal weaning versus immediate extubation [2, 10]. ICU staff members also express concern about choosing the best procedure for mechanical ventilation withdrawal [13, 18, 19].

We designed the prospective observational multicentre ARREVE study to compare immediate extubation versus terminal weaning regarding the long-term presence in relatives of PTSD-related symptoms, complicated grief, and symptoms of anxiety and depression. We also compared comfort of patients during the dying process and well-being of ICU staff members between the two methods.

Methods

Study design

ARREVE was a prospective, observational, multicentre study conducted in 43 French ICUs (in 20 university and 23 non-university hospitals) from February 2013 through April 2014. Critically ill adults (older than 18 years) with a decision to withdraw invasive mechanical ventilation, and the main adult relative of each, were enrolled in the study.

Participating relatives were informed that the clinical data of the patients would be collected and were asked for consent to a phone interview by a psychologist 3, 6, and 12 months after the death. Exclusion criteria for patients were non-invasive ventilation, brain death, and death within 48 h after ICU admission or before the initiation of mechanical ventilation withdrawal; relatives with insufficient knowledge of French for a phone interview and those who declined participation were excluded. Consent to the study was obtained from the relatives after the decision to withdraw mechanical ventilation but before its implementation. For each patient, we included the closest relative among those actively involved in exchanges with the ICU team, as identified by the ICU physicians.

For each patient, we included one nurse, one nursing assistant, one senior ICU physician, and one resident, all of whom had provided care to the patient during the last day before death or ICU discharge. The ethics committee of the French Intensive Care Society (FICS-SRLF) approved the study (see supplementary Appendix).

Terminal weaning and immediate extubation

Immediate extubation consisted in extubation with no previous decrease in ventilatory assistance. Terminal

weaning was defined as a decrease in the amount of ventilatory assistance (oxygen supply and/or tidal volume and/or positive expiratory pressure and/or respiratory rate) and/or as initiation of spontaneous ventilation with a T-piece. The terminal weaning procedure could include the discontinuation of treatments used as adjuncts to mechanical ventilation (i.e. prone position and/or nitric oxide and/or almitrine), and secondary extubation performed in the event of prolonged dying causing distress to the patient and/or the family.

The choice between immediate extubation and terminal weaning was made by the ICU physician and other staff members when withdrawal of mechanical ventilation was decided, according to local practices and preferences of both relatives and ICU staff. Concomitant decisions to withdraw or withhold other treatments were at the discretion of the ICU staff. In this observational study, no specific recommendations were made about end-of-life care, including the use of sedative agents.

Study outcomes

Patient outcomes

Comfort of patients during the dying process was assessed on the basis of both the proportions of patients with airway obstruction and/or gasping and the Behavioural Pain Scale (BPS) score [20].

Psychological assessments of relatives: primary outcome

Relatives were interviewed over the phone by a psychologist 3, 6, and 12 months after the death, with three validated instruments widely used in relatives of ICU patients. The Impact of Events Scale-Revised (IES-R) was completed to assess PTSD-related symptoms 3 and 12 months after the death; scores can range from 0 (no symptoms) to 88 (severe symptoms), and a score greater than 32 indicates PTSD-related symptoms. The IES-R score 3 months after the death was the primary study outcome [8, 21–23].

The Hospital Anxiety and Depression Scale (HADS) includes two subscales for symptoms of anxiety and of depression, respectively. The total score can range from 0 (no anxiety or depression) to 42 (severe anxiety and depression). An anxiety or depression subscore greater than 8 indicates clinically meaningful symptoms [7, 24]. Relatives completed the HADS 3, 6, and 12 months after the death. Finally, the Inventory of Complicated Grief (ICG) was completed by the relatives 6 and 12 months after the death [16, 25]. ICG scores can range from 0 (no complicated grief) to 76, and scores greater than 25 indicate complicated grief.

An additional questionnaire of three general items evaluating the relative's satisfaction with the end of life of the patient was completed during the interview 3 months after the death.

A relative was considered unreachable after 10 unanswered telephone calls. Relatives unreachable 3 months after the death were called 6 months after the death. Relatives who were unreachable 3 and 6 months after the death were not called for the 12-month interview.

Psychological assessments of ICU staff

The ICU staff members completed the Job Strain Score (JSS). This 12-item tool explores three domains (job demand, control, and social support) and has been validated in ICU staff [26, 27]. For each patient, the nurse, nursing assistant, senior physician, and resident included in the study completed the JSS either shortly after the death or on the day of ICU discharge if the patient did not die in the ICU. Total JSS values can range from −3 to 9, with higher scores indicating lower job strain. In addition, each staff member completed a questionnaire of three general items evaluating their satisfaction with the patient's end of life.

Sample size

No reliable data were available for anticipating the IES-R difference between groups. Given the observational design, we planned to perform adjusted analyses and therefore required a number of observations appropriate for the large number of covariates taken into account, i.e. about 40 continuous and 10 qualitative covariates. We consequently planned to recruit 400 relatives in all [28].

Statistical analysis

Continuous variables were reported as mean ± standard deviation (SD) or median and interquartile range (IQR) and categorical variables as number and proportions. Missing data were handled as follows: when a single quantitative item was missing, we imputed the median of observed values for this item then calculated the score; otherwise, we eliminated the relative from the analysis of the relevant outcome measure. The Student test and Chi square test were applied to compare the two groups. Between-group mean differences in scores were estimated, as well as their 95% confidence intervals. Adjusted analyses were performed using linear and logistic regressions. The covariates are listed in the supplementary Appendix. We also performed three sensitivity analyses of the primary outcome, by using a propensity score instead of conventional multivariate analysis, by adding a random centre effect then using a mixed model approach, and by combining these two approaches. Statistical analyses were performed with SAS version 9.2 (SAS Institute, Cary, NC) and R 3.0.2 (http://www.r-project.org).

Results

Characteristics of the patients and relatives

Among 1674 patients treated with mechanical ventilation, 458 patients with a decision to withdraw invasive mechanical ventilation were included (Fig. 1). The distribution of terminal weaning and immediate extubation among the 43 participating centres is shown in eTable 1. We were able to include 190 (90.5%) relatives of the 210 patients with immediate extubation and 212 (85.5%) relatives of the 248 patients with terminal weaning. Demographic characteristics of enrolled relatives did not differ between groups (Table 1).

Patient characteristics are reported in Table 1 and eTable 2. Compared to patients with immediate extubation, more patients with terminal weaning had previous activity limitation, previous ICU admission, surgical diagnosis, and acute respiratory failure at admission. At the time of the withdrawal decision, compared to patients with immediate extubation, those with terminal weaning had a longer ICU stay, worse Sequential Organ Failure Assessment (SOFA) score, greater vasoactive drug use, higher inspired oxygen fraction, and higher end-expiratory pressure.

Decisions to withdraw mechanical ventilation and comfort of patients during the dying process

Compared to relatives in the terminal weaning group, those in the immediate extubation group were more often involved in the withdrawal decision and in choosing between the two methods (eTable 4). Concomitant decisions to withdraw life-sustaining treatments were more common in the terminal weaning group than in the immediate extubation group. Other circumstances surrounding decisions to withdraw mechanical ventilation did not differ between groups.

The dying process is described in Table 2 and eTables 5 and 6. Presence of a relative in the room was twice as common during immediate extubation than during the first step of terminal weaning. Immediate extubation was associated with gasping or symptomatic airway obstruction and with a higher mean BPS score, compared to terminal weaning. Use of opioids, hypnotic drugs, and neuromuscular blocking agents was more common in the terminal weaning group. Secondary extubation was performed eventually in 26 (10.8%) patients receiving terminal weaning, usually because of a prolonged dying process. All patients with terminal weaning died in the ICU, whereas 11 (5.2%) patients were transferred to another ward after immediate extubation. Time to death in the ICU did not differ after terminal weaning initiation and after immediate extubation. Proportions of patients with relatives at their bedside at death in the ICU were similar in both groups.

Psychological variables of relatives in the two groups

Primary outcome

Three months after the death, the mean IES-R score in the relatives was not significantly different between groups. The proportion of relatives with PTSD-related symptoms was also similar (Table 3 and eTables 7–8). These results were unchanged both after adjustment and in the sensitivity analyses.

Secondary outcomes

One year after the death, neither the mean IES-R score nor the frequency of PTSD-related symptoms differed significantly between groups (Table 3 and eTable 7). Similarly, ICG scores showed no significant differences between groups after 6 months or 1 year. Finally, neither the HADS scores nor the frequency of anxiety or depression symptoms was significantly different between groups 3 months, 6 months, or 1 year after the death. Satisfaction of relatives with end-of-life care in the ICU, participation in decisions, and respect of the patient's wishes were high in both groups, with no significant difference (eTable 9).

Psychological variables of ICU staff in the two groups

Total JSS values in the assistant nurses were better with immediate extubation compared to terminal weaning (Table 4 and eTable 10). Total scores for other ICU staff categories were not significantly different between groups. Subscores indicated higher demand in nurses of the terminal weaning group compared to the immediate extubation group. Conversely, higher control and stronger social support were reported in assistant nurses and physicians, respectively, with immediate extubation compared to terminal weaning. Satisfaction of residents with end-of-life care was lower in the immediate extubation group, whereas in the other three ICU staff categories no significant differences were found (eTable 14).

Discussion

This large pragmatic multicentre observational study is the first comparison of immediate extubation versus terminal weaning in terms of quality of death of critically ill patients, as assessed by the comfort of dying in patients and the psychological well-being of relatives and ICU staff. Immediate extubation was associated with greater airway obstruction, a higher frequency of gasping, and higher BPS scores. In the relatives, PTSD-related symptoms, complicated grief, and symptoms of anxiety and depression up to 1 year after the death were not significantly different between the two groups. In the staff, job strain of assistant nurses was lower with immediate extubation compared to terminal weaning.

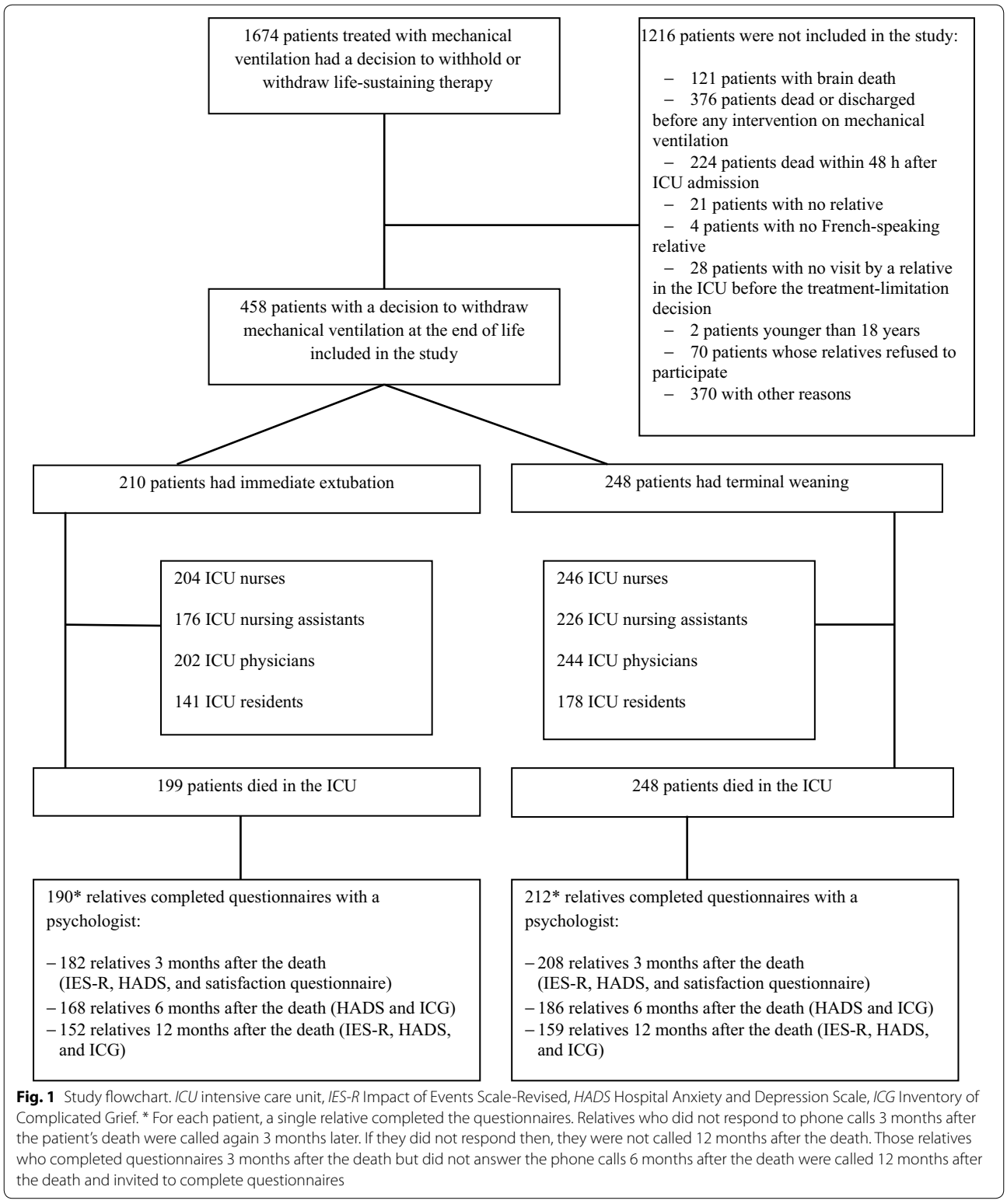

Fig. 1 Study flowchart. *ICU* intensive care unit, *IES-R* Impact of Events Scale-Revised, *HADS* Hospital Anxiety and Depression Scale, *ICG* Inventory of Complicated Grief. * For each patient, a single relative completed the questionnaires. Relatives who did not respond to phone calls 3 months after the patient's death were called again 3 months later. If they did not respond then, they were not called 12 months after the death. Those relatives who completed questionnaires 3 months after the death but did not answer the phone calls 6 months after the death were called 12 months after the death and invited to complete questionnaires

Considerable variation exists in practices for mechanical ventilation withdrawal in the ICU [11, 12]. Few data are available for determining whether one method is superior over the other. Consequently, the choice between the two methods is mainly a matter of opinion. In the current large study under the conditions of everyday practice, immediate extubation and terminal weaning were preferred by nearly identical proportions of ICU staff; however, the

Table 1 Characteristics of the patients and enrolled relatives

Patient characteristics at admission	Immediate extubation *n* = 210	Terminal weaning *n* = 248	*p* value
Age (year), mean ± SD	68 ± 13	67 ± 14	0.53
Male, *n* (%)	122 (58.1)	163 (65.7)	0.09
BMI (kg/m^2), mean ± SD	26.2 ± 5.0	27.3 ± 7.2	0.07
Living arrangements, *n* (%)			0.80
Unknown	1 (0.5)	3 (1.2)	
At home with relative(s)	143 (68.1)	173 (69.8)	
Institutionalised	12 (5.7)	12 (4.8)	
Alone at home	54 (25.7)	60 (24.2)	
Activity limitation (Knaus score)[a], *n* (%)			0.004
A, normal health status	44 (21.0)	37 (15.0)	
B, moderate activity limitation	108 (51.4)	105 (42.5)	
C, severe activity limitation due to chronic disease	50 (23.8)	98 (39.7)	
D, bedridden	8 (3.8)	7 (2.8)	
Chronic diseases, *n* (%)	155 (73.8)	196 (79.0)	0.19
Renal failure	18 (8.6)	28 (11.3)	0.33
Heart failure	10 (4.8)	10 (4.0)	0.70
Liver disease	24 (11.4)	18 (7.3)	0.12
Pulmonary failure	25 (11.9)	43 (17.3)	0.10
Cancer or immunosuppression	49 (23.3)	91 (36.7)	0.002
Diabetes mellitus	46 (21.9)	57 (23.0)	0.78
Neurological disorder	52 (24.8)	55 (22.2)	0.51
Previous ICU stay during current hospital stay, *n* (%)	19 (9.0)	38 (15.3)	0.04
SAPS II[b], mean ± SD	64 ± 15	62 ± 19	0.19
Diagnostic category at ICU admission, *n* (%)			0.04
Medical	192 (91.4)	208 (83.9)	
Scheduled surgery	3 (1.4)	5 (2.0)	
Emergent surgery	15 (7.1)	35 (14.1)	
Diagnosis at ICU admission, *n* (%)			0.002
Sepsis	29 (13.8)	35 (14.1)	
Acute respiratory failure	30 (14.3)	73 (29.4)	
Acute renal failure	2 (1.0)	7 (2.8)	
Cardiac arrest	81 (38.6)	73 (29.4)	
Acute heart failure	5 (2.4)	10 (4.0)	
Acute central neurological failure	35 (16.7)	29 (11.7)	
Multiple trauma	3 (1.4)	3 (1.2)	
Suicide	8 (3.8)	2 (0.8)	
Other	17 (8.1)	16 (6.4)	
Patient characteristics at time of mechanical ventilation withdrawal decision			
ICU stay before decision (days), median [IQR]	6.0 [3.0; 12.0]	8.0 [4.0; 16.5]	<0.001
SOFA[c], mean ± SD	8 ± 4	9 ± 4	<0.001
RASS score[d], mean ± SD	−4 ± 2	−4 ± 1	0.02
Behavioural Pain Scale score[e]	2.5 ± 1.1	2.4 ± 0.8	0.29
Treatments, *n* (%)			
Vasoactive drugs, *n* (%)	34 (16.2)	92 (37.1)	<0.001
Dialysis, *n* (%)	15 (7.1)	28 (11.3)	0.13
FiO_2, mean ± SD	38 ± 18	52 ± 23	<0.001
PEEP (cmH_2O), mean ± SD	5 ± 2	6 ± 3	<0.001
PaO_2/FiO_2, mean ± SD	264 ± 96	209 ± 106	<0.001

Table 1 continued

Relatives' characteristics	*n* = 190	*n* = 212	
Age (year), mean ± SD	54 ± 14	53 ± 14	0.76
Males, *n* (%)	57 (30.2)	62 (29.2)	0.84
Relationship to patient, *n* (%)			0.21
Life partner (married or unmarried)	71 (37.6)	66 (31.1)	
Grown child	87 (46.0)	97 (45.8)	
Parent	3 (1.6)	9 (4.2)	
Other	28 (14.8)	40 (18.9)	
Work status, *n* (%)			0.05
Working	114 (60.3)	111 (52.4)	
Unemployed	9 (4.8)	26 (12.3)	
Retired	59 (31.2)	68 (32.1)	
Other	7 (3.7)	7 (3.3)	
Educational attainment, *n* (%)			0.88
No degree	27 (14.3)	35 (16.6)	
Completed middle school	54 (28.6)	51 (24.2)	
Graduated from high school	34 (18.0)	35 (16.6)	
Bachelor's degree	35 (18.5)	34 (16.1)	
Graduate degree	39 (20.6)	56 (26.5)	
Religion, *n* (%)			0.62
Catholic	115 (60.8)	128 (60.4)	
Muslim	3 (1.6)	7 (3.3)	
Jewish	0 (0.0)	2 (0.9)	
No religion	62 (32.8)	64 (30.2)	
Other	9 (4.8)	11 (5.2)	
Present in the ICU when the patient died, *n* (%)	122 (64.9)	120 (56.6)	0.09

BMI body mass index, *ICU* intensive care unit, *SAPS II* Simplified Acute Physiological Score version II, *SOFA* Sequential Organ Failure Assessment, *RASS* Richmond Agitation Sedation Scale, FiO_2 inspired fraction of oxygen, *PEEP* positive end-expiratory pressure, PaO_2/FiO_2 ratio of arterial oxygen partial pressure over fractional inspired oxygen

[a] Activity levels were defined according to the Knaus chronic health status score: A, previous good health, no functional limitations; B, mild-to-moderate limitation of activity because of a chronic medical problem; C, chronic disease causing serious but not incapacitating limitation of activity; and D, severe restriction of activity due to disease, including being bedridden or institutionalized because of illness [40]

[b] The SAPS II provides a general measure of severity of acute critical illnesses. Values can range from 0 (lowest severity) to 163 (greatest severity, with 100% predicted mortality). A score of 50 predicts 46.1% mortality. The SAPS II was calculated 24 h after ICU admission [41]

[c] The SOFA score provides a measure of organ failure severity. Values can range from 0 (no organ failure) to 24 (greatest severity of multi-organ failure) [42]

[d] The RASS measures levels of sedation and agitation. Values can range from −5 (unrousable patient) to +4 (combative patient). Level 0 indicates an alert and calm patient [43, 44]

[e] The Behavioural Pain Scale measures pain in critically ill patients treated with mechanical ventilation [20]. Three items (facial expression, upper limb movements, and compliance with mechanical ventilation) are scored from 1 to 4. In the current study on withdrawal of mechanical ventilation, the item 'compliance with mechanical ventilation' was not recorded. Therefore, values could range from 2 (no pain) to 8 (severe pain)

between-group differences in admission diagnoses suggest a preference for immediate extubation in comatose patients and for terminal weaning in patients with respiratory failure. In contrast to previously stated opinions, in our observational study, immediate extubation was not associated with a greater burden on the relatives compared to terminal weaning [18]. Importantly, satisfaction was very high among relatives and staff, with no difference between methods, except in the residents. Thus, our study suggests that, for the relatives, the two methods may result in similar experiences, provided the staff members are well trained in, and comfortable with, the method they apply.

Symptomatic airway obstruction and gasps were more common and the mean BPS score was higher in the immediate extubation group. This finding can be ascribed to airway compromise directly related to removal of the endotracheal tube with subsequent obstruction by the tongue and/or inability to remove secretions. Another factor may be underuse of analgesics and sedatives in patients undergoing immediate extubation. Higher doses of opioids and sedatives were used in the patients undergoing terminal weaning, in whom previous respiratory and/or multi-organ failure was more severe than in the immediate extubation group. Interestingly, time to death

Table 2 Assessment of the dying process after the decision to withdraw mechanical ventilation

	Immediate extubation (*N* = 210)	Terminal weaning (*N* = 248)	*p* value
Just before extubation or the first change in ventilator settings for terminal weaning			
Relatives invited to stay in the patient's room during extubation or the first change in ventilator settings for terminal weaning, *n* (%)			<0.001
Accepted	56 (27.5)	114 (46.9)	
Refused	97 (47.5)	62 (25.5)	
Not extended	51 (25.0)	67 (27.6)	
People in the patient's room, *n* (%)			
Senior physician	164 (79.6)	218 (89.3)	0.004
Resident	82 (39.8)	80 (32.9)	0.13
Nurse	205 (99.5)	188 (77.4)	<0.001
Nursing assistant	91 (44.2)	41 (16.9)	<0.001
At least one relative	47 (22.8)	100 (41.2)	<0.001
Religious representative	2 (1.0)	7 (2.9)	0.15
Palliative care team member(s)	0 (0.0)	1 (0.4)	0.36
During the dying process[a]			
Patient's vital signs			
Maximal respiratory rate (/min), mean ± SD	28 ± 10	26 ± 9	0.12
Airway obstruction[b], *n* (%)	138 (65.7)	128 (51.6)	0.002
Gasping, *n* (%)	94 (44.8)	50 (20.2)	<0.001
Highest Behavioural Pain Scale[c] score, mean ± SD	2.9 ± 1.4	2.5 ± 0.9	<0.001
Treatments received			
Opioids, *n* (%)	169 (80.5)	229 (92.3)	<0.001
Highest administration rate (mg/h), mean ± SD	12.4 ± 18.1	23.3 ± 31.5	<0.001
Hypnotic drugs, *n* (%)	154 (73.3)	219 (88.3)	<0.001
Highest administration rate (mg/h), mean ± SD	23.0 ± 49.6	40.2 ± 86.8	0.02
Neuromuscular blocking agents, *n* (%)	4 (1.9)	41 (16.5)	<0.001
At time of death			
Time to death from extubation or first change in ventilator settings for terminal weaning (h), median [IQR]	2.7 [0.4; 10.9]	3.9 [1.0; 17.8]	0.68
Death in the ICU, *n* (%)	199 (94.8)	248 (100.0)	<0.001
Door of the room closed, *n* (%)	128 (68.1)	172 (72.6)	0.31
People in the room, *n* (%)			
Senior physician	62 (32.8)	87 (36.0)	0.49
Resident	32 (17.0)	47 (19.5)	0.51
Nurse	135 (72.2)	156 (64.5)	0.09
Nursing assistant	63 (33.7)	62 (25.8)	0.08
At least one relative	106 (55.2)	139 (57.7)	0.61
Religious representative	2 (1.1)	4 (1.6)	0.70
Palliative care team member(s)	1 (0.5)	0 (0.0)	0.26

The respiratory rates and Behavioural Pain Scale scores in the table are the highest values observed during the dying process

ICU intensive care unit

[a] The dying process was defined as starting at extubation in the immediate extubation group or at the first change in ventilator settings in the terminal weaning group and ending at death

[b] Patients with at least one episode of airway obstruction were recorded. Airway obstruction was assessed using an airway obstruction scale (1, none; 2, mild, without clinical consequences; 3, with one sign of respiratory failure [respiratory rate >30, thoraco-abdominal swing, flaring of the nostrils, or diaphoresis]; and 4, airway obstruction with two or more signs of respiratory failure)

[c] The Behavioural Pain Scale measures pain in critically ill patients treated with mechanical ventilation [20]. Three items (facial expression, upper limb movements, and compliance with mechanical ventilation) are scored from 1 to 4. In the current study on withdrawal of mechanical ventilation, the item 'compliance with mechanical ventilation' was not recorded. Therefore, values could range from 2 (no pain) to 8 (severe pain)

Table 3 Assessment of posttraumatic stress syndrome, complicated grief, anxiety, and depression in relatives after the decision to withdraw mechanical ventilation

	3 months					6 months					12 months				
	Univariate analysis			Multivariate analysis		Univariate analysis			Multivariate analysis		Univariate analysis			Multivariate analysis	
	Extubation *N* = 182	Terminal weaning *N* = 208	*P* value		*P* value	Extubation *N* = 168	Terminal weaning *N* = 186	*p* value		*p* value	Immediate extubation *N* = 152	Terminal weaning *N* = 159	*p* value		*p* value
IES-R[a], mean ± SD												*N* = 158[d]			
Total score	30.5 ± 16.2	31.9 ± 18.1				–	–		–		23.6 ± 17.1	25.0 ± 16.4			
Estimated difference [95% CI]	−1.4 [−4.8; 2.0]		0.43	−1.9 [−5.9; 2.1]	0.36						−1.4 [−5.1; 2.3]		0.46	−0.8 [−5.2; 3.6]	0.72
Intrusion	14.8 ± 7.5	15.7 ± 7.7				–	–		–		11.4 ± 7.7	12.7 ± 7.2			
Estimated difference [95% CI]	−0.9 [−2.4; 0.6]		0.25	−1.0 [−2.8; 0.8]	0.26						−1.3 [−3.0; 0.3]		0.12	−1.2 [−3.2; 0.8]	0.24
Hyperarousal	5.8 ± 5.5	5.8 ± 5.9				–	–		–		5.1 ± 5.3	5.2 ± 5.1			
Estimated difference [95% CI]	−0.0 [−1.2; 1.1]		0.89	−0.1 [−1.4; 1.3]	0.93						−0.1 [−1.2; 1.1]		0.97	0.5 [−0.9; 1.9]	0.46
Avoidance	9.9 ± 7.1	10.4 ± 7.2				–	–		–		7.1 ± 6.8	7.2 ± 6.8			
Estimated difference [95% CI]	−0.5 [−1.8; 1.0]		0.57	−0.8 [−2.5; 0.9]	0.37						−0.1 [−1.6; 1.5]		0.94	−0.1 [−2.0; 1.7]	0.88
Presence of PTSD-related symptoms, *n* (%)	84 (46.2)	89 (42.8)		–		–	–		–		40 (26.3)	50 (31.6)			
Odds ratio [95% CI]	1.15 [0.77; 1.71]		0.50	1.18 [0.70; 1.99]	0.54						0.77 [0.47; 1.26]		0.30	0.86 [0.44; 1.67]	0.64
ICG[b], mean ± SD															
Total score	–	–		–		22.4 ± 14.6	23.7 ± 15.0				21.0 ± 16.1	19.6 ± 14.2			
Estimated difference [95% CI]						−1.3 [−4.4; 1.8]		0.42	0.0 [−3.6; 3.5]	0.99	1.4 [−2.0; 4.8]		0.42	1.6 [−2.3; 5.6]	0.42
Presence of complicated grief symptoms, *n* (%)	–	–		–		58 (34.5)	80 (43.0)				55 (36.2)	54 (34.0)			
Odds ratio [95% CI]						0.70 [0.45; 1.07]		0.10	0.67 [0.37; 1.22]	0.19	1.10 [0.69; 1.76]		0.68	1.07 [0.57; 2.02]	0.83

Table 3 continued

	3 months					6 months					12 months				
	Univariate analysis			Multivariate analysis		Univariate analysis			Multivariate analysis		Univariate analysis			Multivariate analysis	
	Extubation *N* = 182	Terminal weaning *N* = 208	*P* value		*P* value	Extubation *N* = 168	Terminal weaning *N* = 186	*p* value		*p* value	Immediate extubation *N* = 152	Terminal weaning *N* = 159	*p* value		*p* value
HADS[c], mean ± SD															
Total score	15.3 ± 8.6	14.2 ± 9.1				12.8 ± 8.4	12.4 ± 8.3				11.7 ± 8.1	10.9 ± 7.3			
Estimated difference [95% CI]	1.1 [−0.7; 2.9]		0.22	0.8 [−1.2; 2.8]	0.42	0.4 [−1.3; 2.2]		0.62	1.7 [−0.4; 3.7]	0.11	0.8 [−0.9; 2.5]		0.35	1.4 [−0.7; 3.4]	0.19
Anxiety	8.2 ± 4.6	7.9 ± 4.9				7.6 ± 4.7	7.5 ± 4.8				7.3 ± 4.5	6.9 ± 4.2			
Estimated difference [95% CI]	0.3 [−0.7; 1.3]		0.55	0.2 [−0.9; 1.3]	0.75	0.1 [-0.8; 1.2]		0.73	0.8 [−0.4; 2.0]	0.19	0.4 [−0.6; 1.4]		0.42	0.6 [−0.6; 1.8]	0.30
Depression	7.1 ± 5.3	6.2 ± 5.5				5.2 ± 5.0	4.9 ± 4.8				4.5 ± 4.6	4.0 ± 4.2			
Estimated difference [95% CI]	0.8 [−0.3; 1.9]		0.13	0.7 [−0.6; 1.9]	0.29	0.3 [−0.8; 1.3]		0.61	0.9 [−0.3; 2.1]	0.15	0.5 [−0.6; 1.4]		0.41	0.8 [−0.4; 2.0]	0.22
Presence of anxiety symptoms, *n* (%)	76 (41.8)	87 (41.8)				70 (41.7)	73 (39.2)				50 (32.9)	49 (30.8)			
Odds ratio [95% CI]	0.99 [0.67; 1.45]		0.99	1.01 [0.60; 1.69]	0.97	1.10 [0.72; 1.69]		0.64	1.26 [0.72; 2.20]	0.42	1.10 [0.68; 1.77]		0.69	1.26 [0.67; 2.39]	0.48
Presence of depression symptoms, *n* (%)	72 (39.6)	63 (30.3)				42 (25.0)	41 (22.0)				26 (17.1)	21 (13.2)			
Odds ratio [95% CI]	1.50 [0.99; 2.29]		0.06	1.53 [0.89; 2.64]	0.13	1.18 [0.72; 1.93]		0.51	1.68 [0.87; 3.23]	0.12	1.36 [0.73; 2.53]		0.34	1.51 [0.68; 3.38]	0.32

IES-R Impact of Events Scale-Revised, *95% CI* 95% confidence interval, *PTSD* posttraumatic stress syndrome, *ICG* Inventory of Complicated Grief, *HADS* Hospital Anxiety and Depression Scale

[a] Total scores on the Impact of Events Scale-Revised (IES-R) can range from 0 (no PTSD-related symptoms) to 88 (severe PTSD-related symptoms). A total IES-R score >32 indicates PTSD-related symptoms. The intrusion subscore can range from 0 to 32, the hyperarousal subscore from 0 to 24, and the avoidance subscore from 0 to 32

[b] The Inventory of Complicated Grief (ICG) score can range from 0 (no complicated grief) to 76. Scores >25 indicate complicated grief

[c] The Hospital Anxiety and Depression Scale score can range from 0 (no anxiety or depression) to 42 (severe anxiety and depression). Anxiety or depression subscores >8 indicate clinically meaningful symptoms of anxiety or depression, respectively

[d] One relative had six unanswered items and was not included in the analysis

Table 4 Job Strain Scores of nurses, nursing assistants, senior physicians, and residents

	Nurses		p	Nursing assistants		p	Senior physicians		p	Residents		p
	Multivariate analysis											
	Immediate extubation	Terminal weaning		Immediate extubation	Terminal weaning		Immediate extubation	Terminal weaning		Immediate extubation	Terminal weaning	
	n = 195	*n* = 241		*n* = 164	*n* = 215		*n* = 201	*n* = 231		*n* = 141	*n* = 175	
				Multivariate analysis			Multivariate analysis			Multivariate analysis		
Job Strain Score												
Estimated difference [95% CI]	0.1 [−0.3; 0.5]		0.55	0.6 [0.2; 1.0]		0.01	0.3 [0.0; 0.7]		0.07	0.1 [−0.3; 0.5]		0.54
Demand												
Estimated difference [95% CI]	−0.2 [−0.4; 0.0]		0.02	−0.1 [−0.3; 0.1]		0.41	0.1 [−0.1; 0.2]		0.54	−0.1 [−0.3; 0.1]		0.21
Control												
Estimated difference [95% CI]	−0.1 [−0.3; 0.2]		0.54	0.3 [0.1; 0.5]		0.02	0.2 [0.0; 0.4]		0.11	−0.1 [−0.4; 0.2]		0.52
Social support												
Estimated difference [95% CI]	0.0 [−0.2; 0.2]		0.83	0.2 [0.0; 0.4]		0.06	0.2 [0.0; 0.4]		0.02	0.1 [−0.1; 0.3]		0.21

The Job Strain Score measures the degree of job strain by exploring three domains (job demand, control, and social support). The Job Strain Score is obtained by adding the control and social support subscores, then subtracting the demand subscore [(social support + control) − demand]. Total scores can range from −3 to 9. Higher scores indicate less job strain

from extubation or first change in ventilator settings for terminal weaning did not differ between groups, in keeping with previous findings [29]. Conceivably, physicians may be concerned about active shortening of the dying process related to pre-emptive deep sedation after extubation [30]. On the other hand, in the terminal weaning group, the greater use of opioids and sedatives, and the administration to some patients of neuromuscular blocking agents, may reflect a willingness to shorten the dying process, despite the double-effect principle and guidelines discouraging the use of neuromuscular blocking agents at the end of life [31, 32]. Both hypotheses suggest room for improving end-of-life care. However, the use of neuromuscular blockade may also reflect an attempt by ICU staff to avoid additional suffering in relatives of patients who are deeply comatose with severe myoclonic status epilepticus or distressing agonal gasps despite high doses of sedative drugs [32].

Finally, we found that the psychological welfare of the ICU staff was better with immediate extubation than with terminal weaning. The emotional responses of staff members to death may affect their beliefs about whether withdrawing life support is legitimate and whether comfort care should be offered as an option [33]. Differences in perceptions of the two methods have been reported, but their associations with markers for psychological burden in staff members had not been evaluated previously [13, 14, 18]. In ICU nurses, both caring for dying patients and the number of decisions to forego life-sustaining treatments are associated with increased burnout, which may also influence nurses' beliefs and behaviours [34]. In a recent study of ICU staff perceptions, a preference for terminal weaning was related to an unfavourable perception of immediate extubation, whereas both staff members who preferred extubation and those with no preference perceived extubation as providing a less medicalised death and minimising ambiguity [18]. Thus, identifying personal beliefs that might constitute barriers to mechanical ventilation withdrawal is crucial when seeking to implement protocols for patient care [35–38].

The main limitation of this study is the absence of randomisation. However, a major concern when performing end-of-life studies with psychological assessments of relatives and staff is the risk of adverse effects induced by modifying the usual practice of the ICUs in a direction contrary to the convictions of the participating ICU teams. Indeed, ICU staff members differ in their perceptions of immediate extubation and terminal weaning, suggesting a risk of poor compliance with random allocation of the method of mechanical ventilation withdrawal [19]. Another limitation is that end-of-life care was not standardised, as shown by the differences in this regard between the two groups. However, dictating end-of-life practices for the study might have generated bias due to reluctance of ICU staff to apply methods with which they felt uncomfortable. Moreover, we used a clear definition of terminal weaning and immediate extubation. Immediate extubation was not preceded by interventions on ventilator settings and very few patients in the terminal weaning group underwent secondary extubation. These conditions avoided any mismatch between the two practices. Last, neither the adjusted nor the sensitivity analyses suggested any associations linking the patients' baseline characteristics or end-of-life practices to the study results. A third limitation is that communication between ICU staff and relatives was not evaluated in detail, and no specific recommendations were provided. Studies have emphasised the importance of good communication with relatives of dying patients [16, 39]. However, as previously stated, our aim was to interfere as little as possible with the everyday practice of the ICU teams. The absence of difference in psychological welfare of relatives between groups suggests that communication between ICU staff and relatives in both groups was in line with patient health state. The fourth limitation is that all participating ICUs were in France. Whether our findings apply to other countries is unclear. However, the ICUs were distributed throughout France and located in both university and community hospitals. Moreover, frequencies and levels of PTSD-related symptoms, complicated grief, and symptoms of anxiety and depression in the relatives were consistent with previous reports [6]. Last, the large size and varied case-mix of our patient population support the general applicability of our findings to other countries and settings.

In conclusion, immediate extubation for mechanical ventilation withdrawal was not associated with differences in psychological welfare of relatives compared to terminal weaning, when each method constituted standard practice in the ICU where it was applied. Compared to terminal weaning, immediate extubation was associated with less job strain in ICU staff. Patients had more airway obstruction and gasps with immediate extubation, indicating a need for better palliative care.

Electronic supplementary material

The online version of this article (doi:10.1007/s00134-017-4891-0) contains supplementary material, which is available to authorized users.

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Acknowledgements
We are indebted to Celine Deletage, Carole Guignon, Stéphanie Martin, and Vanessa Zinzoni who monitored the study; Isabelle Treillet and Cedric Colombo, the psychologists who performed the interviews; and A. Wolfe, MD, who helped to prepare and review the manuscript. We are grateful to all medical staff, staff nurses, and research nurses at the 43 sites for their valuable contribution to the success of the study.

Additional contributions
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Compliance with ethical standards

Conflicts of interest
The authors declare that they have no conflict of interest.

Funding
The ARREVE study was supported by grants from three non-profit organisations: the Fondation de France (#000332577), La Roche-sur-Yon Departmental Hospital, and Programme Hospitalier de Recherche Clinique National 2012 of the French Ministry of Health (#13-0142).

Received: 2 May 2017 Accepted: 18 July 2017
Published online: 22 September 2017

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