# The effect of extubation failure on outcome in a multidisciplinary Australian intensive care unit

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## ABSTRACT

**Background:** A reported association between extubation failure (EF) and increased hospital length of stay and mortality led us to assess outcome of EF in an Australian intensive care unit.

**Design and setting:** Non-interventional cohort study in the intensive care/high dependency unit of a tertiary referral hospital, 2000–2003.

**Methods:** EF was defined as reintubation within 72 hours of extubation. Causes of EF were determined by review of the clinical notes and prospective record of the EF event. Patients were excluded if they were aged $\leqslant$ 14 years, self-extubated, were reintubated to replace a defective endotracheal tube, or had been extubated but were returning to the operating theatre. Physiological variables used to calculate severity of illness score were analysed to ascertain correlation with EF.

**Results:** 2761 patients were electively extubated, and 52 (1.8%) fulfilled the criteria for EF. Compared with those successfully extubated, EF patients had a higher 24 h APACHE II score (18.0 ± 7.0 [mean ± SD] v 15.3 ± 7.4, $P = 0.009$), significant increases in length of stay in ICU (12.8 ± 8.3 v 3.0 ± 6.0 days, $P < 0.001$) and hospital (33.5 ± 40.8 v 18.0 ± 28.6 days, $P < 0.001$) and tracheostomy rate (38.5% v 3.5%, $P < 0.001$).The commonest cause of EF was excess secretions or aspiration (32%). EF was independently associated with hospital mortality (odds ratio [OR], 2.10; 95% CI, 1.00–4.41; $P = 0.048$) and low serum albumin level on admission (OR, 0.75; 95% CI, 0.55–1.00; $P = 0.05$). Neither aetiology of airway failure (OR, 2.21; 95% CI, 0.56–8.75; $P = 0.25$) nor time to reintubation (OR, 0.99; 95% CI, 0.97–1.01; $P = 0.76$) were associated with mortality.

**Conclusion:** Our findings confirm an increased risk of adverse outcomes for patients with EF. We observed a comparatively low EF rate. Confirmation in similar patient cohorts is required.


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Extubation failure (EF) has been associated with prolongation of intensive care unit and hospital stay. It has also been associated with increased hospital mortality, after controlling for severity of illness and comorbid conditions, in some but not all studies.[1,2] Time to reintubation and aetiology of EF have also been associated with mortality.[3]

The increased risk of adverse outcomes may have a number of causes, including the direct consequences of reintubation, the prolonged ventilation that follows, or the clinical deterioration that occurs from the time of extubation until reintubation. Alternatively EF may simply be a marker of underlying severity of illness.[3]

There are few outcome data on EF from Australasia. To determine whether the above outcomes occur in Australasian patients with EF we undertook a non-interventional cohort study in an Australian ICU.

## Methods

### Study population

We evaluated patients admitted to the Intensive Care Unit/High Dependency Unit at The Canberra Hospital, Australian Capital Territory, between January 2000 and December 2003. The ACT Department of Health and Community Care Human Research Ethics Committee was notified and agreed to the use of de-identified data. During the study period, the facility was staffed as 10-bed medical and surgical ICU/HDU serving both an adult and paediatric population. The hospital did not perform solid organ transplantation but was a major trauma referral centre. Forty per cent of admissions were elective post-surgical patients, including post-cardiac surgical patients.

The study excluded patients aged 14 years and younger, patients who self-extubated, those who were reintubated to replace a defective endotracheal tube, and those who had been extubated but were returning to the operating theatre for another procedure. No minimum intubation time was required and, unlike some studies which excluded certain diagnostic groups,[4] the study included all patients irrespective of the reason for tracheal intubation.

### Extubation and reintubation criteria

All decisions regarding ventilator weaning, including its timing, mode and rate, were made by the ICU medical team led by an intensivist. Weaning protocols and objective weaning indices were not used. Decisions were based on clinical judgement combined with arterial blood gas analysis. General criteria for weaning and extubation included adequate reversal of the underlying disease process, intact respiratory drive, freedom

**Table 1. Patient characteristics and outcomes compared between patients with extubation failure and those who were successfully extubated***

| | Failed extubation ($n = 52$) | Successful extubation ($n = 2709$) | $P$ |
|---|---|---|---|
| **Patient characteristics** | | | |
| No. of males | 36 (69%) | 1729 (63%) | 0.42 |
| Age (years) | 60.0 ± 19.0 | 59.0 ± 17.6 | 0.69 |
| APACHE II score | 18.0 ± 7.0 | 15.3 ± 7.4 | 0.009 |
| SAPS II score | 37.9 ± 13.3 | 34.1 ± 15.9 | 0.18 |
| **Outcomes** | | | |
| Length of stay (days) | | | |
| ICU | 12.8 ± 8.3 | 3.0 ± 6.0 | < 0.001 |
| Hospital | 33.5 ± 40.8 | 18.0 ± 28.6 | < 0.001 |
| Deaths | | | |
| ICU | 9 (17.3%) | 312 (11.5%) | 0.19 |
| Hospital | 14 (27.0%) | 446 (16.5%) | 0.05 |
| Tracheostomy | 20 (38.5%) | 97 (3.5%) | < 0.001 |
| Ventilation time (h)† | 92.0 ± 105.0 | 62.4 ± 100.0 | 0.002 |

* Data are mean ± SD unless otherwise stated.
† Ventilation time before extubation.

from sedatives and neuromuscular blocking agents, adequate airway reflexes, adequate cough, minimal respiratory secretions, alert mental status and stable circulation.

Weaning was accomplished by reducing the intermittent ventilation rate and level of pressure support. Patients were extubated after attainment of either low levels of pressure support ($\leqslant$ 10 cm$H_2O$), positive end-expiratory pressure ($\leqslant$ 8 cm$H_2O$) and oxygen ($FIO_2 \leqslant 40\%$), or a successful 30–120-minute spontaneous breathing trial.

Reintubation was based on clinical judgement. General criteria included inability to manage secretion load or upper airway obstruction, manifesting as stridor, progressive respiratory failure, or intercurrent events (eg, acute pulmonary oedema).

## Data collection and definitions

Data on all patients admitted to the ICU were extracted from the ICU databases and patient clinical record. Data included diagnosis, demographic characteristics, hospital and ICU admission(s) and discharges, date and time of each intubation and reintubation, and ICU and hospital mortality. Routinely collected clinical, physiological and laboratory data for the first 24 hours of ICU admission were also extracted from the ICU ANZICS AORTIC database. These included laboratory and physiological parameters (worst, highest and lowest) used to calculate the 24-hour APACHE II[5] and SAPS II[6] scores.

Episodes of EF and the direct cause were recorded prospectively by one author (JW). To ensure that reintubation was most likely to have been intentional and temporally related to the recent course of mechanical ventilation, EF was defined as the requirement for reintubation within 72 hours of extubation.[1] The EF cohort was selected by retrospectively excluding all patients who fell outside this time limit.

Aetiology of EF was classified as airway or non-airway,[3] based on the prospective record of the EF event and review of the clinical notes. Airway causes included upper airway obstruction (stridor corrected by reintubation), aspiration and excess pulmonary secretions (defined as secretions sufficient to cause clinically evident airway obstruction or aspiration). Non-airway causes were cardiovascular, neurological (encephalopathy reducing the level of consciousness) and respiratory (increased work of breathing accompanied by hypoxaemia [$SpO_2 \leqslant 90\%$ or $PaO_2 \leqslant 60$ mmHg while receiving $FIO_2 \geqslant 0.5$, or increase in $PaCO_2 \geqslant 10$ mmHg from pre-extubation level]). When more than one aetiology existed, the cause that precipitated reintubation, as judged by the clinical team, was identified as predominant.

## Statistical analysis

The primary outcome measures were ICU and hospital length of stay and hospital mortality, adjusted for severity of illness, compared between patients with EF and those who were successfully extubated. Secondary outcome measures were the type of EF (airway or non-airway) and time to reintubation in relation to hospital mortality, and the relationship between physiological variables used to calculate the 24-hour severity of illness scores and EF.

**Table 2. Aetiology of extubation failure (EF), indexed to hospital death**

| | Patients | | Hospital deaths | |
|---|---|---|---|---|
| Aetiology of EF | No. | % of EF patients | No. | % of patients* |
| **Airway ($n = 27$)** | | | | |
| Aspiration/excess secretions | 17 | 32% | 6 | 35% |
| Upper airway obstruction | 10 | 19% | 3 | 30% |
| **Non-airway ($n = 23$)** | | | | |
| Respiratory | 12 | 23% | 2 | 16% |
| Cardiovascular | 7 | 13% | 2 | 28% |
| Neurological/ encephalopathy | 4 | 7% | 1 | 25% |
| **Mixed/unknown ($n = 2$)** | 2 | 4% | 0 | 0 |

* Deaths as a percentage of patients with specific EF aetiology.

**Table 3. Patient outcomes according to aetiology of extubation failure***

| | Non-airway ($n=23$) | Airway ($n=27$) | $P$ |
|---|---|---|---|
| Age (years) | 63.9±16.1 | 58.7±20.8 | 0.33 |
| Length of stay (days) | | | |
| ICU | 12.5±9.6 | 13.4±7.2 | 0.71 |
| Hospital | 25.0±15.0 | 42.0±54.0 | 0.15 |
| Deaths | | | |
| ICU | 3 (13%) | 6 (22%) | 0.39 |
| Hospital | 5 (21%) | 9 (33%) | 0.36 |
| APACHE II score | 17.3±6.6 | 18.0± 6.1 | 0.69 |
| Tracheostomy | 2 (8.6%) | 18 (66%) | <0.001 |
| Duration (h) | | | |
| 1st intubation | 83.3±123.0 | 94.5±82.0 | 0.70 |
| Extubation to reintubation | 33.7±35.0 | 30.2±36.0 | 0.73 |
| 2nd intubation | 108±78 | 70.1±51 | 0.04 |

* Aetiology could not be classified for two patients. Data are mean±SD unless otherwise stated.

Continuous variables were compared with Student's two tailed *t* test, while non-continuous or categorical variables were compared with the $\chi^2$ test (Pearson's test or Fisher's two-tailed exact test). A $P$ value <0.05 was considered significant. Values were expressed as mean±SD or absolute percentage. Logistic regression analysis was used to calculate adjusted odds ratios and was performed on data for all extubated patients, separately for those with EF, and to determine significance of physiological variables. Statistical analyses were performed using SPSS version 12.0.1 (SPPS Inc, Chicago, Ill, USA) and STATA version 8.2 (Statacorp, College Station, Tex, USA).

## Results

Over the 4-year study period, 4393 patients were admitted to the ICU/HDU facility. After exclusion criteria were applied, 2761 patients were identified as having been extubated electively: 52 of these (1.8%) fulfilled the criteria for EF, while 2709 were successfully extubated. Outcome data on excluded patients were not analysed.

Demographic characteristics and outcomes are compared between patients with EF and those who were successfully extubated in Table 1. The EF group had a significantly higher APACHE II score on admission to the ICU (18.0±7.0 versus 15.3±7.4; $P=0.009$), but no difference in SAPS II score. No age or sex differences were noted between the groups.

Compared with successful extubation, EF was associated with significantly longer ICU and hospital stays (12.8±8.3 versus 3.0±6.0 days, $P<0.001$ for ICU stay; and 33.5±40.8 versus 18.0±28.6 days, $P<0.001$ for hospital stay). No difference in unadjusted ICU mortality was observed, but unadjusted hospital mortality was higher in those with EF (27.0% versus 16.5%, $P=0.05$). EF was associated with a significantly higher tracheostomy rate (38.5% versus 3.5%, $P<0.001$) and mechanical ventilation time before extubation (92.0±105.0 versus 62.4±100.0 hours, $P=0.002$) compared with those successfully extubated.

Aetiology of EF is shown in Table 2. Aetiology was classified as airway in 27 (52%) patients and non-airway in 23 (44%) patients, and could not be classified in two patients. The predominant airway causes of EF were excess secretion load and/or aspiration, noted in 17 (32%) cases, and upper airway obstruction in 10 (19%). The predominant non-airway causes were respiratory failure in 12 (23%) patients, cardiovascular in seven (13%), and encephalopathy/neurological in four (7%).

Outcome according to aetiology of EF is shown in Table 3. There was no overall difference noted between patients with airway causes and those with non-airway causes in ICU or hospital length of stay, or ICU or hospital mortality. Compared with those with non-airway aetiology, those with an airway cause had a significantly higher tracheostomy rate (66% versus 8.6%, $P<0.001$) and significantly shorter duration of the second intubation (70.1±51 versus 108.0±78 hours, $P=0.04$), but no difference in duration of first intubation nor time from extubation to reintubation. When time to reintubation was <2 hours (eight cases), stridor was immediately evident in four patients.

**Table 4. Comparison of patients who survived and those who died after extubation failure***

| | Survived ($n=38$) | Died ($n=14$) | $P$ |
|---|---|---|---|
| No. of males (%) | 27 (71%) | 9 (64%) | 0.63 |
| APACHE II score | 17.5±7.2 | 19.5±6.3 | 0.37 |
| SAPS II score | 36.5±14.0 | 41.4±10.7 | 0.24 |
| Age (years) | 57.0±19.0 | 70.0±12.0 | 0.03 |
| Length of stay (days) | | | |
| ICU | 12.1±8.2 | 14.6±8.6 | 0.34 |
| Hospital | 38.3±46.2 | 20.5±13.5 | 0.16 |
| Tracheostomy (%) | 14 (36%) | 6 (42%) | 0.70 |
| Duration (h) | | | |
| 1st intubation | 83.4±108 | 116±98 | 0.32 |
| Extubation to reintubation | 29.5±33.6 | 33.2±39.0 | 0.74 |
| 2nd intubation | 90.8±71.6 | 72.6±50.0 | 0.38 |

* Data are mean±SD unless otherwise stated.

**Table 5. Diagnostic categories in patients with extubation failure ($n = 52$)**

| Diagnosis | No. of patients |
|---|---|
| Trauma (head and multiple) | 10 (19%) |
| Cardiac surgery | 10 (19%) |
| Abdominal aortic aneurysm (acute) | 6 (11%) |
| Postoperative | 7 (13%) |
| Pneumonia | 5 (9%) |
| Shock (non-septic) | 4 (7%) |
| Exacerbated chronic obstructive pulmonary disease | 3 (5%) |
| Acute pulmonary oedema | 2 (5%) |
| Other | 3 (5%) |

Survivors and non-survivors of EF are compared in Table 4. Fourteen patients with EF (26%) died, and 38 (73%) survived. Those who survived were significantly younger than those who died (57.0 ± 19.0 versus 70.0 ± 12 years, $P$= 0.03), but no significant differences were noted in sex, APACHE II or SAPS II score, ICU or hospital length of stay, or tracheostomy rate between the two groups. Nor was any significant difference observed in time to reintubation between those who survived and those who died (29.5 ± 33.6 versus 33.2 ± 39.0 hours, $P = 0.74$).

Diagnostic categories in patients with EF are shown in Table 5. Cardiac surgery and trauma patients comprised 38% of the total.

### Multivariate analysis

The first multivariate analysis examined all 2761 patients who were extubated. The independent variables entered into the analysis were EF and APACHE II (or SAPS II) score. The dependent variable was hospital mortality. We found that APACHE II score (adjusted odds ratio [OR], 1.25; 95% CI, 1.22–1.27; $P < 0.001$) and SAPS II score (adjusted OR, 1.12; 95% CI, 1.11–1.13; $P < 0.001$) were both independently associated with hospital mortality. When adjusted for severity of illness, EF remained independently associated with hospital mortality (adjusted OR, 2.10; 95% CI, 1.00–4.41; $P = 0.048$).

The second multivariate analysis examined the 52 patients with EF. The independent variables entered into the analysis were SAPS II score, APACHE II score, age, aetiology of airway failure (airway or non-airway), time to reintubation, and duration of first intubation. The dependent variable was hospital mortality. After adjustment for all other confounding variables, age at admission was the only variable that remained independently associated with hospital death (adjusted OR, 1.05; 95% CI, 1.00–1.10; $P = 0.04$). Cause of airway failure (adjusted OR, 2.21; 95% CI, 0.56–8.75; $P$= 0.25), time to reintubation (adjusted OR, 0.99; 95% CI, 0.97–1.01; $P = 0.76$) and duration of first intubation (adjusted OR, 1.00; 95% CI, 0.99–1.00; $P = 0.35$) were all unrelated to hospital mortality.

Adjusted odds ratios for the association between 24-hour physiological variables and EF are shown in Table 6. Highest heart rate and lowest serum albumin level within the first 24 hours of admission were the only variables independently associated with EF in the multivariate model.

## Discussion

This study showed that EF was associated with several adverse outcomes for patients in a large multidisciplinary Australian ICU, including increases in both hospital and ICU stay, tracheostomy rate and severity of illness-adjusted hospital mortality. While comparative Australasian outcome data are lacking, these results appear consistent with previously published studies from Europe and North America.[1,4,7]

The prolongation of both ICU and hospital length of stay (in our study by 9 days in the ICU and 15 days in the hospital) has been shown to depend on a number of variables, including patient case mix and aetiology of the EF event.[2] Although we reported a significantly shorter duration for the second intubation in those with airway as opposed to non-airway EF (70 versus 108 hours), this made no difference to overall ICU and hospital stays, suggesting that reasons other than airway control existed for patients staying in the ICU. Length of stay may also be prolonged by the complications of reintubation, including effects of prolonged sedation or mechanical ventilation, particularly ventilator-associated pneumonia.[8] Finally, increased ICU and hospital length of stay will result in an inevitable increase in hospital costs, varyingly reported as between 20% and 50% above baseline.[4,9]

**Table 6. Physiological variables in the first 24 hours in ICU associated with extubation failure**

| Variable | Adjusted odds ratio (95% CI) | $P$ |
|---|---|---|
| Highest heart rate | 1.65 (1.36–1.99) | < 0.001 |
| Lowest heart rate | 1.44 (1.06–1.94) | 0.01 |
| Lowest serum albumin level | 0.71 (0.53–0.95) | 0.02 |
| Lowest serum potassium level | 0.74 (0.57–0.97) | 0.03 |
| Highest mean arterial pressure | 1.32 (1.06–1.65) | 0.01 |
| Highest systolic blood pressure | 1.30 (1.07–1.57) | 0.007 |
| Highest diastolic blood pressure | 1.27 (1.00–1.62) | 0.05 |
| **Highest heart rate*** | **1.49 (1.15–1.95)** | **0.003** |
| **Lowest serum albumin level*** | **0.75 (0.55–1.00)** | **0.05** |

* Variables that remained independently associated after adjusting for confounding variables are shown in bold.

An increase in hospital mortality has been noted in some but not all studies of EF.[10] The increase is a feature of both planned and unplanned EF, and patients who successfully tolerate unplanned extubation do not have increased mortality.[11] The increased mortality may relate to the particular patient cohort studied. We observed a twofold increase in hospital mortality after adjustment for severity of illness in a largely unselected mixed patient cohort. Daley et al,[12] in a predominantly trauma cohort, found no increase in mortality with EF, but patients in this cohort were predominantly young and had no limiting physiological disturbance. In contrast, Epstein et al reported a sevenfold increase in mortality after EF in an older medical cohort with significant comorbidities.[1]

The exact cause of the increased mortality accompanying EF is unclear. It does not seem simply an effect of more severe illness, as the association persisted after adjustment for severity of illness and comorbid conditions in our study and others.[13] Mortality might also be a direct result of the effects or complications of the reintubation process itself, but evidence supporting this is weak.[12] There is more substantial support for the concept that poor outcome results from the adverse effects of prolonged mechanical ventilation, particularly ventilator-associated pneumonia.[8] Finally, and of most clinical interest, is the proposal that clinical deterioration may occur between the time of extubation and reintubation, allowing organ failure to establish. However, after controlling for the aetiology of EF and illness severity, we did not find a relationship between time to reintubation and hospital mortality. Nevertheless, this relationship has been previously demonstrated in several patient cohorts, including respiratory patients, whose mortality doubled when reintubation was delayed beyond 13 hours,[14] and medical patients who showed a sequential increase in mortality (24% to 69%) when reintubation was delayed from a baseline of 0–12 hours up to 72 hours.[3] In that study, EF survivors had mechanical ventilation reinstated an average of 15 hours ahead of non-survivors.[3] The clinical implication is that delay in re-establishing mechanical ventilation may increase mortality.

Mortality in EF may also relate to the aetiology of the EF event itself and may be independently lower in those with an airway cause for EF compared with a non-airway cause.[3] Presumably, the mortality advantage for those who require reintubation for a purely airway reason (eg, stridor caused by laryngeal oedema) relates to easily correctable abnormalities which would not be expected to increase mortality if promptly corrected. This contrasts with some forms of non-airway EF (eg, cardiac failure and encephalopathy) which may represent perturbations of organ function and inherently carry a poor prognosis. Our study showed that, although 65% of the EF patients who died had an airway cause, after adjustment for confounding variables, there was no significant difference in hospital mortality between airway and non-airway EF.

Although one might expect the time to reintubation to be shorter in patients with an airway cause for EF, we found that the mean time to reintubation did not differ significantly between the two types of EF, at around 30 hours, consistent with the findings of others.[1] This may in part have been reflective of the criteria used to define airway failure, which included excess or retained secretions which may take longer to manifest. Patients with EF due to airway causes had a significantly shorter duration for the second intubation (70 versus 108 hours), suggesting the abnormality was quickly corrected (eg, oedema). With prolonged intubation, the incidence of tracheal pathology increases (eg, granuloma and ulcer), but the relationship between intubation time and EF is unclear.[15,16] Although overall those with EF had longer mechanical ventilation times before their index extubation than those without EF, if a relationship was to be evident one might expect those with EF for airway reasons to have a longer duration of first intubation. This was not evident in our study, but might reflect the way we classified EF, or the small patient numbers.

The incidence of EF has been reported as 2% to 25%, depending on the patient cohort. Medical, paediatric and multidisciplinary ICU patients seem at highest risk, and cardiothoracic, general surgical and trauma patients generally at the lowest risk.[10,12,17] Considering our patient case mix, we found a comparatively low rate of EF (1.8%). However, there are few data from other Australasian ICUs for comparison, although one study examining weaning methodology also reported an EF rate of 1.8%.[18] Plausible explanations for our low EF rate include inherent differences in the way many large Australian ICUs are managed, with a predominance of certified intensivists, one-to-one ratios of nurses to ventilated patients, and a "closed unit" type structure, with management supervised by intensivists. Not only would this be expected to produce a more consistent approach to weaning and extubation, but these systems in themselves have been noted to improve outcomes and to reduce risk of EF.[13,19,20] There may also be inherent differences in the way mechanically ventilated patients are managed between continents. Data on unplanned extubation rates hint at this, with rates in some European and American centres reported at 11%–17% per patient, as opposed to Australian rates of 0.4%.[21] However, further confirmatory outcome studies are needed before any firm conclusions can be drawn.

While several physiological variables have been associated with EF, including low haemoglobin level and raised blood urea nitrogen level,[22,23] we found that only low serum albumin level and highest heart rate in the first 24 hours correlated independently with EF. The correlation with low serum albumin level on ICU admission is expected, as nutritional depletion or severe perturbations in organ function may place patients at greater risk of EF. Hypoalbuminaemia was similarly shown to correlate with EF in elderly patients admitted with respiratory failure, presumably reflecting generalised severity of illness and premorbid nutritional status, and has also been associated with EF in post-cardiac surgical patients.[23,24] However, the clinical relevance of this finding in our study is limited. Despite the association with EF, many patients who were successfully extubated also had a low serum albumin level, reducing its predictive utility (data not shown). In addition, the results reflect the first 24 hours of admission only. It would have been useful to correlate these variables with EF at the time of the index extubation.

Our study had a number of limitations. Firstly, although EF was prospectively recorded by a single observer, the EF cohort was selected and the aetiology of EF determined retrospectively by note review, limiting predictive utility. As physiological measurements at ICU admission may not correlate with those at the time of extubation, analysis may have had more clinical relevance if we had examined data from both the time of admission and just before extubation. In addition, the design of the study may be open to criticism. A more accurate analysis may have been possible by examining and comparing a smaller number of successfully extubated patients (case–control), as in some other studies.[2] Nevertheless, to our knowledge, our study is the first to report in detail the outcome from EF in Australian intensive care practice.

## Conclusion

Our study confirms the adverse outcomes for patients with EF. These include significant prolongation of ICU and hospital length of stay, and doubling of hospital mortality after adjustment for severity of illness. EF rate was low considering the patient cohort, and further confirmatory studies from comparable institutions are needed.

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