Prediction of death after withdrawal of life-sustaining treatments

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ABSTRACT

Objective: To assess the predictive value of respiratory and haemodynamic variables and opinion of the intensivist for determining how soon death occurs after withdrawal of life-sustaining treatments (WLST).

Design: Multicentre prospective observational study.

Participants and setting: 83 consecutive adult intensive care patients at John Hunter and Calvary Mater Hospitals, Newcastle, New South Wales, for whom a decision was made to withdraw life-sustaining treatment between March 2007 and March 2008.

Main outcome measures: Data were collected before initiation of palliation. Primary outcome was to recognise in a multivariate analysis the parameters associated with a time to death ⩽ 60 minutes after WLST.

Results: 81 patients underwent WLST: 79 died, and two survived to be discharged from hospital. Thirty-six patients (45%) died within 60 minutes of WLST, and 45 (55%) survived 60 minutes or longer. Mean ICU stay before WLST was 4.8 days (range, 1–85 days). Mean time from WLST to death was 6:31 h (range, 1 minute to 31 days). A modified University of Wisconsin assessment tool showed no statistical association with the time from WLST to death ($P = 0.09$). The adapted United Network for Organ Sharing tool, systolic blood pressure, APACHE II score, ventilatory dependence, oxygen disruption, Glasgow Coma Scale (GCS) score and staff specialist opinion all showed a statistically significant association with time from WLST to death ($P < 0.05$).

Conclusions: It is possible to predict the time from WLST to death accurately using a tool that combines GCS, respiratory and haemodynamic parameters and intensivist opinion. These results require validation in a large multicentre study.

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Withdrawal of life-sustaining treatments (WLST) on ethical, legal and medical grounds has become established over the past decades and is common practice not only in Australian intensive care units, but around the globe. Up to 13.5% and 19% of patients admitted to ICUs in Europe and the United States, respectively, have some form of life-sustaining treatment withdrawn, typically mechanical ventilation.[1,2]

In Australia, guidelines and recommendations have been published to regulate and guide this practice.[3,4] Therapeutic failure remains the most common reason for WLST. Other frequently documented reasons are meaningless outcome due to poor prognosis, and patient's autonomy as perceived by the treating physician or based on documentation of advanced directives.[5]

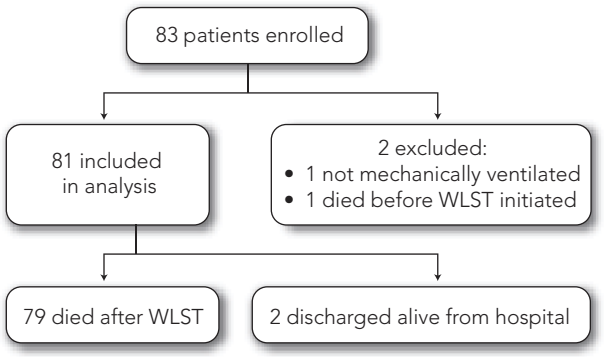
Although experience with WLST and palliative care has been growing, some aspects remain uncertain, such as the time from extubation to death. The duration of this period can have a major impact on the family's grieving and understanding of the process, on the allocation of intensive care resources and, more recently, on the prospect of organ donation after death.[6]

The practice of WLST varies widely, and the reported time from WLST to death depends on the therapies actively ceased, the patient's respiratory, neurological and haemodynamic condition, and the reasons for WLST.[7-12] Reported times range from minutes to hours, with a small percentage of patients surviving to be discharged from hospital.[2,13-15] The period is very important in determining the suitability of patients for organ donation after circulatory arrest (donation after cardiac death). Only when death occurs within a particular "organ-specific" time (30 to 90 minutes) can the patient be considered for donation, because of the limited acceptable warm ischaemic times.[6]

Tools currently available to predict this timing are those from the University of Wisconsin (UW)[16] and the United Network of Organ Sharing (UNOS).[17] Both are numerical scales created to assess the likelihood of prolonged survival after extubation,[16] and both rely on a trial of spontaneous respiratory rate and oxygenation when the patient is disconnected from mechanical ventilation. However, in Australia, any intervention during WLST that is not directed at improving the palliative care provided is considered medically and ethically inappropriate.[6] In the absence of a spontaneous breathing trial, the UW and UNOS tools may be poor predictors of survival time.

The aim of this study was to evaluate the predictive value of the UW and UNOS tools in the absence of any ventilatory intervention, as well as the value of intensivists' opinion of likely survival time after WLST.

Figure 1. Flowchart of patients prospectively enrolled in the study



WLST = Withdrawal of life-sustaining treatments.

Methods

This was a multicentre prospective study conducted at the John Hunter Hospital and Calvary Mater Hospital, Newcastle, New South Wales, between March 2007 and March 2008. All adult patients who underwent WLST were eligible for the study. Patients diagnosed with brain death and those who had treatment limitation only were excluded.

Therapies considered life-sustaining were invasive mechanical ventilation, oxygen supplementation, vasopressor and inotrope infusion, cardiac pacing, external circulatory support, intra-aortic balloon pump (IABP), and renal replacement therapy (intermittent or continuous).

The process of WLST was initiated by the intensivist in consensus with other medical officers and family members, consistent with NSW *End-of-life care and decision-making — guidelines*.[4]

Immediately before WLST, the staff specialist notified a research coordinator or investigator and completed a case report form, which included the adapted UW and UNOS scoring tools, demographic data, respiratory and cardiovascular parameters and laboratory data, as well as the staff specialist's opinion as to whether death would occur within 60 minutes. Palliative care was initiated soon afterwards.

The UW tool scores body mass index, number of vasopressor infusions, patient age, route of intubation, respiratory rate, negative inspiratory force, tidal volume and oxygen saturation after disconnection from mechanical ventilation for 10 minutes. The higher the score, the lower the probability of breathing spontaneously after extubation.

The UNOS tool is a composite score that includes the use of a ventricular assist device, IABP and extracorporeal membrane oxygenation (ECMO), pacemaker-unassisted heart rate < 30 beats/min, dose of noradrenaline, phenylephrine, dopamine and dobutamine, as well as oxygen saturation in relation to positive end-expiratory pressure

Table 1. Baseline characteristics of the 81 study patients

Characteristic	No. or mean ±SD	% or range
Sex		
No. of men	46	57%
No. of women	35	43%
Age	66.1 ±15.2	29–89
APACHE II score	26.5 ±8.9	9–62
Body mass index (kg/m^2)	26.7 ±5.4	14.1–43.0
Temperature (° C)	36.5 ±1.3	34.0–41.0
Glasgow Coma Scale	4.7 ±3.0	3–15
ICU days	4.8 ±9.8	1–85
Mean time of day for WLST	14:20	5:35–22:50
Time from WLST to death	6:31 ±11:58 h	1 min–31 days
Access for mechanical ventilation		
Endotracheal tube	77	95%
Tracheostomy	4	5%
Haemodynamic status		
Systolic blood pressure	124 ±33.9	59–240
Diastolic blood pressure	63 ±17.5	12–111
Heart rate	91.8 ±19.2	50–150
Vasopressors other than vasopressin		
No	50	62%
Yes	31	38%
Inotropes		
No	68	84%
Yes	13	16%
Cardiac pacing		
Yes	2	2%
No	79	98%
Vasopressin		
Yes	13	16%
No	68	84%
Urinary output		
Normal	39	48%
Polyuria*	10	12%
Oliguria	15	19%
Anuria	17	21%
Ventilator dependent†		
Yes	32	40%
No	49	61%
Disruption in oxygenation‡		
Yes	16	20%
No	65	80%
Survival time after WLST		
⩽ 60 minutes	36	45%
> 60 minutes	45§	56%

WLST = withdrawal of life-sustaining treatments.
* Polyuria defined as urinary output > 200 mL/h.
† Spontaneous respiratory effort that triggered the ventilator cycle < 8 or > 30 per minute.
‡ SaO_2 < 92% with a PEEP > 10 cmH_2O or an FIO_2 > 0.5.
§ Two patients survived to hospital discharge.

(PEEP) and fraction of inspired oxygen (F_{IO_2}). The UNOS tool also scores the spontaneous respiratory rate during a trial off mechanical ventilation.

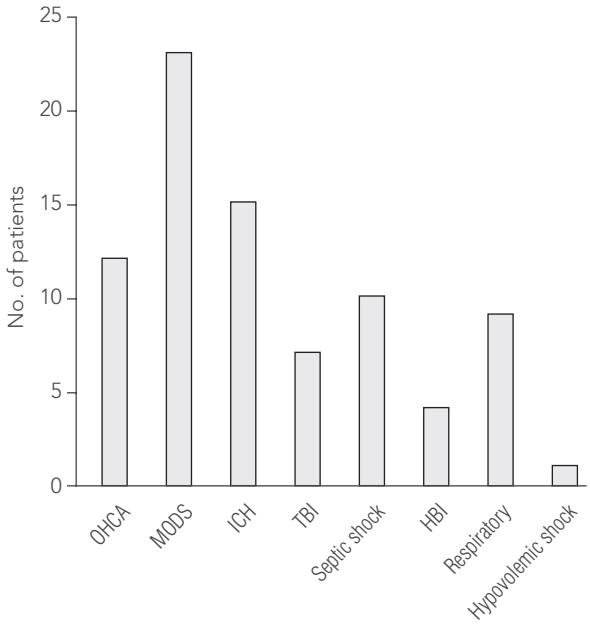
For our study, we adapted the UW and UNOS scores to avoid disconnecting the patient from mechanical ventilation. We defined ventilator dependence as a rate of spontaneous respiratory effort that triggered the ventilator cycle of less than 8 or more than 30 per minute. We defined oxygen disruption as $Sa_{O_2} < 92\%$ with a PEEP $> 10\ cmH_2O$ or an $F_{IO_2} > 0.5$ at the time of extubation.

Patients were followed up until death or discharge from hospital. Primary outcome was to recognise through a multivariate analysis all clinical parameters associated with a period from WLST to cardiorespiratory arrest of less than 60 minutes.

Statistical analysis

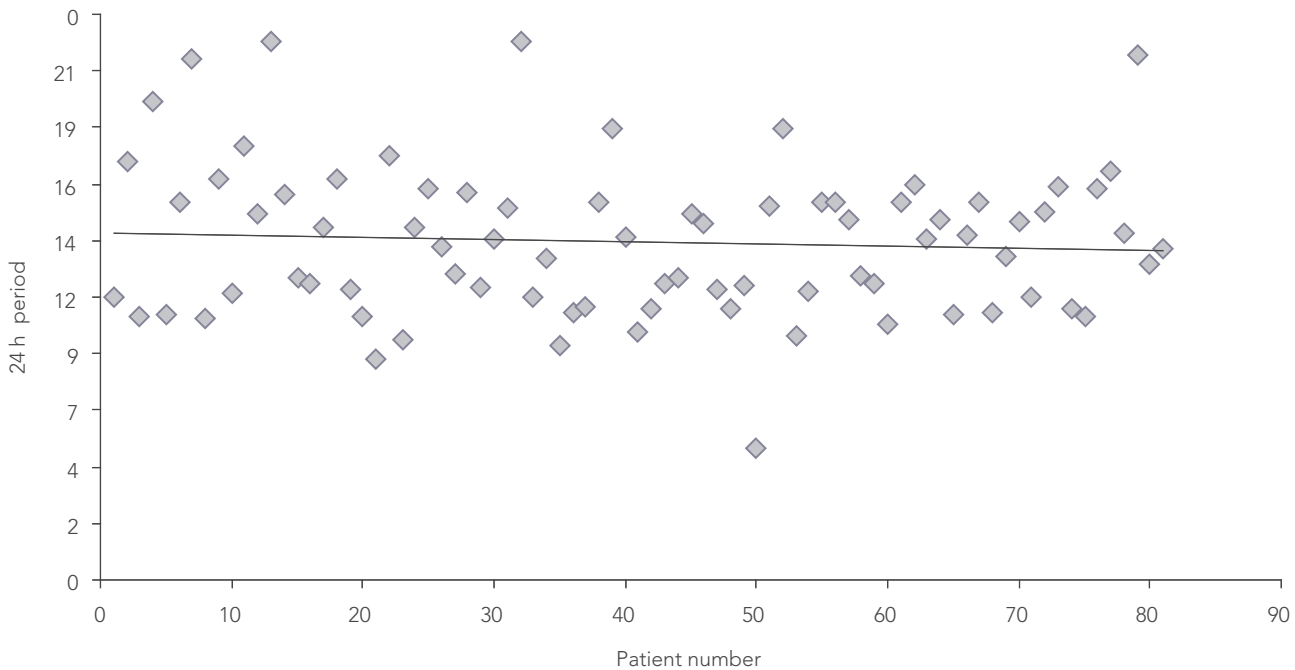
To evaluate the possible association between a risk or predictor and the outcome, all categorical independent variables with more than two values were analysed with Fisher's exact test. All continuous independent data were analysed with *t* tests. When values less than 5 were identified in any cell, those variables were grouped to meet Cochran's criteria. A *P* less than 0.05 was considered statistically significant for a difference between samples. Binary logistic regression analysis (odds ratio, 95% CI) was used to test for any significant association between out-

Figure 2. Leading reasons for withdrawal of life-sustaining treatments in the ICU



OHCA = out of hospital cardiac arrest.
MODS = multi-organ dysfunction syndrome.
ICH = intracerebral haemorrhage. TBI = traumatic brain injury.
HBI = hypoxaemic brain injury.

Figure 3. Time of the day when withdrawal of life-sustaining treatments was initiated*



*The solid line represents the mean.

come and predictive tools. Positive and negative predictive values were obtained. SPSS version 15.0 for Windows (SPSS Inc, Chicago, Ill) was use for the analysis.

The study was approved by the Hunter New England Area Research Ethics Committee. Consent was not required from patients or their next-of-kin, as this was an observational study that did not affect patient care.

Results

Between March 2007 and March 2008, 83 intensive care patients underwent WLST and were eligible for the study. Two of these were excluded: one was not undergoing mechanical ventilation at the time of WLST, and the other died before WLST was implemented (Figure 1). Data were analysed for 81 patients: 79 of these died after WLST, and two were discharged from hospital alive.

Baseline characteristics of the 81 patients are shown in Table 1. Mean APACHE II score was 26.5 ±8.9. The mean time from admission to WLST was 4.8 days (range, 1–85 days). The most common reason for WLST was therapeutic failure after multiorgan dysfunction syndrome (MODS) (23, 28%), followed by intracerebral haemorrhage (15, 19%), out-of-hospital cardiac arrest (12, 15%) and septic shock (10, 12%) (Figure 2). Hypoxaemic brain injury (HBI) from causes other than cardiac arrest was categorised separately. WLST was most common in the early afternoon (Figure 3). Mean time from WLST to death was 6:31 h (range,1 minute to 31 days), excluding the two patients discharged alive.

Of the 81 patients, 36 (45%) died within 60 minutes of WLST, and 45 (55%) survived longer than 60 minutes (Table 1). There were no significant differences between the two groups in sex, age, body mass index, temperature, cardiac rhythm or rate, diastolic blood pressure, use of inotropic support or access route for mechanical ventilation (Table 2).

The adapted UW tool was a poor predictor of the time from WLST to death, with a positive predictive value of 57.6% and a negative predictive value of 61.8%. The medical leading cause for WLST was not associated with time to death ($P = 0.63$). On the other hand, mean systolic blood pressure ($P < 0.001$), APACHE II score ($P = 0.008$), use of vasopressors ($P = 0.03$), ventilatory dependence ($P = 0.003$), disruption in oxygenation ($P = 0.006$) and the modified UNOS predicting tool ($P < 0.001$) were all significantly associated with time to death. Staff specialist opinion was strongly associated with time to death ⩽60 minutes ($P < 0.001$), with specificity and sensitivity of 77.7% and 88.9%, respectively, giving a positive predictive value of 76.1% and a negative predictive value of 89.7%. Use of vasopressin was analysed separately from use of other vasopressors and was not a statistically significant predictor

Table 2. Significance of demographic, haemodynamic and respiratory factors associated with the time from WLST to death

	⩽60 min ($n = 36$)	>60 min ($n = 45$)	*P*
Sex			0.82
Male	21	25	
Female	15	20	
Age	68.2 ±14.7	64.5 ±15.5	0.46
APACHE II score	30.8 ±10.6	25.3 ±6.5	0.008
Body mass index (kg/m^2)	26.2 ±4.0	27.2 ±6.4	0.39
Temperature (° C)	36.8 ±1.5	37.3 ±1.1	0.09
Haemodynamics			
Systolic blood pressure	109.4 ±32.6	135.7 ±30.5	<0.001
Diastolic blood pressure	56.6 ±34.4	68.1 ±24.8	0.09
Heart rate	94.4 ±20.0	89.8 ±18.5	0.55
Vasopressors	21	10	0.03
Inotropes	9	4	0.13
Pacing	1	1	1.0
Vasopressin	8	5	0.37
Cardiac rhythm			
Sinus rhythm	15	28	0.34
Atrial fibrillation	6	8	1.0
Sinus tachycardia	14	8	0.14
Respiratory			
Endotracheal tube	35	42	1.0
Tracheostomy	1	3	0.62
Ventilatory dependence*			0.003
Yes	22	10	
No	14	35	
Oxygen disruption†			0.006
Yes	12	4	
No	24	41	
Staff specialist opinion			<0.001
Yes	32	10	
No	4	35	
Glasgow Coma Scale	3.9 ±2.5	5.5 ±3.2	0.01
UW tool			0.09
Low	15	11	
Moderate	21	33	
High	0	1	
UNOS tool			<0.001
Very low	11	3	
Low	11	4	
Moderate	7	11	
High	7	27	

UW = University of Wisconsin.
UNOS = United Network for Organ Sharing.
* Spontaneous respiratory effort that triggered the ventilator cycle <8 or >30 per minute.
† SaO_2 <92% with a PEEP of >10 cmH_2O or an FIO_2 >0.5.

Table 3. Logistic regression analysis

	Sensitivity	Specificity	PPV	NPV
UW tool	41.6%	75.5%	57.6%	61.8%
UNOS score*	61.1%	84.4%	75.8%	73.0%
Hunter New England Area composite†				
⩽ 2 variables	55.5%	13.3%	33.8%	27.2%
⩾ 3 variables	38.8%	95.5%	87.5%	66.1%

PPV = positive predictive value. NPV = negative predictive value.
UW = University of Wisconsin.
UNOS = United Network for Organ Sharing.
* Score was grouped as very low/low and moderate/high risk.
† Hunter New England Area composite included either two variables (ventilatory dependence + oxygen disruption) or three variables (ventilatory dependence + oxygen disruption + systolic blood pressure < 100 mmHg).

($P = 0.37$). The modified UNOS tool had a positive predictive value of 75.8% and a negative predictive value of 73.0%.

Multivariate logistic regression showed no significant association between the time to death and the adapted UW tool (odds ratio [OR], 0.42; 95% CI, 0.15–1.14), but the association with the modified UNOS tool reached statistical significance (OR, 4.9; 95% CI, 1.38–17.6). A local composite score that included ventilator dependence, oxygen disruption and systolic blood pressure < 100 mmHg had a specificity of 95.5% and a positive predictive value of 87.5% when three or more components were present (Table 3).

Data on the potential for donation after cardiac death were collected prospectively: 37 patients (46%) had abnormal liver function, and 40 (49%) and 37 (46%) had abnormal urea and creatinine levels, respectively. Forty-one had exclusion criteria for donation after cardiac death: 12 (29%) had a history of carcinoma, 21 (51%) had uncontrolled sepsis, five (12%) had viral hepatitis, and three (7%) belonged to a high-risk group for HIV infection, such as injecting drug user, recent imprisonment, recent needlestick injury, or sexual contact with a high-risk partner.

Twenty-two patients were not reported by the staff specialist. Analysis of baseline characteristics and all further analyses found no significant differences between the groups or the final results.

Discussion

We found that 45% of our patients died within 60 minutes of WLST. A similar study by DeVita et al reported the same percentage.[17] Keenan et al[14] reported in a retrospective cohort that 55% of their patients died within 1 hour, and 98% by the end of the first day. These results differ from the findings of Revelly et al[13] that only 22% of ventilated patients died within an hour. However, they did not report either the haemodynamic support at the time of extubation or respiratory parameters, and could not identify variables that predicted timing. The same problem is seen in the report of a selected group of non-heart-beating donors by DeVita et al,[15] in which 80% of the patients died in less than 20 minutes.

The UNOS tool for predicting time to death showed a positive predictive value of 82% in the study of DeVita et al,[17] compared with 75.8% in our study. These findings would probably eliminate the need for disconnection from mechanical ventilation in the UNOS test. The UW tool was based on only 43 cases and was reported to predict death within 60 minutes in 84%. In our group of patients, it had a positive predictive value of 57.6%.

In our study, mechanical ventilation, oxygen supplementation and vasopressors were the therapies most frequently ceased at the time of WLST, which is similar to the finding in the extensive reports in the literature.[5,7,9,11,12,14] The average time from WLST to death in our patients was 6.3 hours — also similar to the experience of Revelly et al,[13] with a mean reported time of 4.8 hours. Other published experience reveals times from 2.4 hours to 1.8 days.[5,7-10]

The largest study to date that has collected information on modalities and demographics after WLST is the Ethicus Trial, reported by Sprung et al.[1] This prospective study in 17 European countries reported a median time from admission to WLST of 4 days, with 89% of patients dying within 48 hours. Yazigi et al[11] reported a median time of 5 days from admission to WLST, with 93% of the patients dying in the ICU; similarly, Ferrand et al[12] reported 94.7% of deaths occurring in the ICU. ICU day stays from 2 to 6.1 days were reported by Eidelman et al,[8] Wunsch et al[10] and Nolin and Andersson,[5] with up to 94.8% of the patients dying in the ICU after WLST. In our population, patients were in the ICU an average of 4.8 days before the decision was made for WLST, with a hospital mortality of 97.4% in the first 2 days.

Nolin and Andersson[5] reported therapeutic failure and MODS as the most common reasons for WLST. These findings were consistent with those of Yazigi et al.[11] Our results were also consistent, as failure to respond to therapy after MODS triggered most of the end-of-life decisions.

In our population, WLST occurred almost invariably in the afternoon. It seems that, after agreement is reached with family members and other medical officers, the time of WLST is carefully planned. This has also been reported by Keenan et al.[14]

To our knowledge, there is only one mention in the literature of a relationship between APACHE II score and time from WLST to death.[10] We found that patients with a higher severity score on admission had a shorter time from extubation to cardiocirculatory arrest.

Of interest is the phenomenon of patients surviving to be discharged from hospital after WLTS. In our study, two patients survived to hospital discharge, one having been readmitted to the rehabilitation ward. This phenomenon has been reported previously by Cook et al[2] and Wunsch at al[10] in Canada, the US and the United Kingdom, where up to 3.6% of patients were discharged from hospital after discontinuation of mechanical ventilation during WLST. Esteban et al[9] reported that 2.2% patients were discharged alive, while Nolin and Andersson[5] reported 7.2%. Although never investigated in detail, some patients in this group could have had changes to the end-of-life decision, re-initiation of therapy, or perhaps clinical judgements were imprecise.

In our experience, low systolic blood pressure and the use of vasopressors were most strongly related to the likelihood of dying within 60 minutes of WLST. The lack of a significant association between the use of inotropes and timing to death after WLST might be a result of the small numbers. Ventilatory parameters and oxygenation disruption also correlated with the time to death. This seems biologically plausible, as cardiocirculatory arrest is ultimately a consequence of tissue hypoxia in the setting of WLST.

Although statistically significant, the difference in mean GCS score between the group who died within 60 minutes of WLST and the group who died later (3.9 v 5.5) could be difficult to interpret clinically, and its impact on a clinical tool is debatable.

Staff specialist opinion was a very strong predictor of death within 60 minutes of WLST, but we did not investigate the variables that contributed to that opinion. We assume they included most of the variables that we assessed, creating a problem for the analysis given the overlap of information. We decided to maintain that opinion is a subjective parameter that needed to be balanced with the objective parameters observed.

When we included information on the biochemical, haemodynamic and other characteristics of patients who underwent WLST to assess their suitability as organ donors after cardiac death, few would have qualified. The number might have increased slightly if renal exclusions were more flexible. This makes the process of predicting time to death even more important to avoid the patient's family having false expectations, as well as to trigger the appropriate process. However, this study was not designed to identify potential organ donors.

Although the study did not aim to determine the mean dose of sedatives and analgesia used in palliative care, it found that the mean dose of morphine was 2.4 mg/h, and the mean dose of midazolam was 2.1 mg/h. The Ethicus Study found higher mean doses: 13.4 mg/h for morphine and 13.8 mg/h for midazolam. However, that study included a group of patients who underwent "shortening of the dying process" as part of end-of-life practices.

Our study had some limitations. First, some patients were not enrolled in the study because of under-reporting, potentially leading to selection bias. However, the patient sample was enrolled by staff specialists who were representative of all staff specialists working in the ICUs. We also analysed the missed patients separately and found no significant differences in their baseline characteristics or results. We did not use the UW and UNOS tools exactly as published, as we omitted the trial of withdrawal of mechanical ventilation; thus, their positive or negative predictive values cannot be extrapolated exactly from the literature. Remarkably, it seems that if the degree of ventilatory support and the oxygenation demand are assessed without intervention, the sensitivity of the UNOS tool remains reasonable.

In conclusion, we demonstrated that about 45% of ICU patients who have life-sustaining treatment withdrawn reach cardiorespiratory arrest within 60 minutes. This group can be predicted from a composite tool that includes haemodynamic and respiratory variables and staff specialist opinion. A large multicentre study is needed to validate this tool, which could potentially be applied generally in Australian and New Zealand ICUs.

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References

1 Sprung C, Cohen S, Sjokvist P, et al. End-of-life practices in European intensive care units. The Ethicus Study. *JAMA* 2003; 290: 790-7.
2 Cook D, Rocker G, Marshall J, et al. Withdrawal of mechanical ventilation in anticipation of death in the intensive care unit. *N Engl J Med* 2003; 349: 1123-32.
3 Australian and New Zealand Intensive Care Society. Statement on withholding and withdrawing treatment. Melbourne: ANZICS, 2003.

4 New South Wales Government Department of Health. End-of-life care and decision-making — guidelines. Sydney: The Department, 2005. (File No. 03/4776-2.)
5 Nolin T, Andersson R. Withdrawal of medical treatment in the ICU. A cohort study of 318 cases during 1994–2000. *Acta Anaesthesiol Scand* 2003; 47: 501-7.
6 NSW Health Department. Organ donation after cardiac death. Health and research and ethics. Sydney: NSW Department of Health, 2007. (File No 04/3586-2.)
7 Wood G, Martin E. Withholding and withdrawing life-sustaining therapy in a Canadian intensive care unit. *Can J Anaesth* 1995; 42: 186-91.
8 Eidelman L, Jakobson D, Pizov R, et al. Forgoing life-sustaining treatment in an Israeli ICU. *Intensive Care Med* 1998; 24: 162-6.
9 Esteban A, Gordo F, Solsona J, et al. Withdrawing and withholding life support in the intensive care unit: a Spanish prospective multicentre observational study. *Intensive Care Med* 2001; 27: 1744-9.
10 Wunsch H, Harrison D, Harvey S, Rowan K. End-of-life decisions: a cohort study of the withdrawal of all active treatment in the intensive care units in the United Kingdom. *Intensive Care Med* 2005; 31: 823-31.
11 Yazigi A, Riachi M, Dabbar G. Withholding and withdrawal of life-sustaining treatment in a Lebanese intensive care unit: a prospective observational study. *Intensive Care Med* 2005; 31: 562-7.
12 Ferrand E, Robert R, Ingrant P, Lemaire F. Withholding and withdrawal of life support in intensive care units in France: a prospective survey. *Lancet* 2001; 357: 9-14.
13 Revelly JP, Imperatori L, Maravic P, et al. Are terminally ill dying in the ICU suitable for non-heart beating organ donation? *Intensive Care Med* 2006; 32: 708-12.
14 Keenan S, Busche K, Chen L, et al. A retrospective review of a large cohort of patients undergoing the process of withholding or withdrawal of life support. *Crit Care Med* 1997; 25: 1324-31.
15 Devita M, Snyder J, Arnold R, Siminoff L. Observations of withdrawal of life-sustaining treatment from patients who became non-heart beating donors. *Crit Care Med* 2000; 28: 1709-12.
16 Lewis J, Peltier J, Nelson H, et al. Development of the University of Wisconsin Donation After Cardiac Death Evaluation Tool. *Progress Transplant* 2003; 13: 265-73.
17 DeVita M, Brooks M, Zawistowski C, et al. Donors after cardiac death: validation of the Identification Criteria (DVIC) Study for Predictors of Rapid Death. *Am J Transplantation* 2008; 8: 432-41.❑