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A validated rule for predicting patients who require prolonged ventilation post cardiac surgery

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Abstract

Objective: Prolonged ventilation post surgery causes logistic problems on cardiac surgical intensive care units (CSU). We thus sought to derive and validate a clinical decision rule to predict patients at high risk of prolonged ventilation, so that the timing of operations on high risk patients can be optimised in the context of the workload of the CSU. **Methods**: The North Staffordshire Royal Infirmary (NSRI) Open Heart Registry was analysed from April 1998 to May 2002. Prolonged ventilation was defined as that which was longer than 24 h. The Parsonnet score was assessed for its ability to predict these patients. Univariate analysis was first performed to identify predictive variables. Recursive partitioning and logistic regression was then performed to identify the optimal decision rule. This rule was then validated on the Blackpool Victoria Hospital (BVH) Open Heart Registry. **Results**: A total of 3070 patients were analysed of whom 201 were ventilated for more than 24 h. A Parsonnet score of 10 predicted 49% of high risk patients but 618 low risk patients are misclassified. Our rule that uses Parsonnet score over 7, ejection fraction, operation status, PA pressure and age, to identify high risk patients identifies 50% of those needing prolonged ventilation and only incorrectly identifies 282 of the 2869 patients with normal ventilation times giving a specificity of over 90%. Validation in the BVH database demonstrated similar findings. **Conclusion**: Our rule identifies 14% of all our patients as high risk and 50% of these required prolonged ventilation. Such a rule allows more efficient use of scarce CSU resources by appropriate surgical scheduling.

Keywords: Thoracic surgery; Ventilation; Postoperative complications; Decision making; Clinical protocols

1. Introduction

Most patients are extubated within 6–8 h after cardiac surgery. However, a significant number of patients continue to receive mechanical ventilation for prolonged periods. Rates of around 5–8% remaining ventilated above 24–48 h have been reported [1–3]. This has major implications for the progress of patients through the Cardiac Surgical Intensive Care Unit (CSU) and, in busy cardiac centres, operations are regularly cancelled due to the lack of bed-space in the CSU due to patients requiring prolonged ventilation. In contrast, units will often have spare bed-space over the weekend or at other times in the year, when reduced numbers of operations being performed means that if beds are spare, potential capacity is wasted. Therefore if the patients who require prolonged ventilation could be predicted preoperatively, then their operations could be planned for periods least likely to cause over-occupancy in the CSU.

Several studies have attempted to identify preoperative risk factors for prolonged ventilation [2–7], However, no study has yet described a validated predictive rule or score that will robustly predict those patients likely to require prolonged ventilation.

The aim of our study was therefore to derive and validate a clinical decision rule that would identify a cohort of patients that were at high risk of prolonged ventilation, so that the timing of their operation can be optimally planned in the context of limited intensive care resources.

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2. Methods

2.1. Design

This was an observational cohort study.

2.2. Setting

Patient records were analysed from the North Staffordshire Royal Infirmary Open Heart Registry from March 1998 to May 2002. This is a UK centre performing 900 operations per year in the Midlands. This data was used to derive the decision rule. Patient records were then analysed from the Blackpool Victoria Hospital Open Heart Registry from January 1996 to December 1999. This is a centre of similar size in the North-West of England. This data was used to assess the external validity of the derived rule.

2.3. Subjects and outcome measures

All patients undergoing a Cardiac surgical procedure were included in the study. All clinical variables were prospectively collected according to guidelines for the UK national dataset and all independent variables were defined according to these recommendations [8].

The dependent variable was ventilation of over 24 h, as recorded by the Intensive care staff. The ventilation time was defined as the time from arriving in the Intensive care unit to the time of extubation. It is our experience that the recording of this data is highly reliable and consistent in both units. Twenty-four hours was selected by us as we felt this would be the most clinically useful cohort of patients for us to identify as opposed to alternative longer or shorter time periods. If a patient was reintubated, we considered that this would likely to be due to a new complication and thus we did not add this time to the original intubation time. Any clinical variable that had more than 1% missing data was excluded from the study.

2.4. Data analysis

Univariate analysis was initially used to determine the strength of association between each variable and the primary outcome to aid selection of variables for multivariate analyses. The North Staffordshire database was used for this analysis. Initial univariate analysis was performed on categorical data using the Pearson Chi-squared test or Fisher's exact test where any expected cell count was less than 5. Continuous variables were analysed using the unpaired Student *t*-test where a Gaussian distribution could be demonstrated. The remaining data, and variables containing rank data was analysed using the Mann–Whitney *U*-test. Univariate analysis and logistic regression was performed using SPSS version 11.5 [9]

Multivariate analysis was conducted using both logistic regression and recursive partitioning to find the best combinations of predictor variables that were highly sensitive for detecting the outcome measure whilst also achieving the maximum possible specificity. Regression model building proceeded with forward stepwise selection until no variables met the entry ($P < 0.05$) or removal ($P < 0.10$) criteria for the significance level of the likelihood-ratio test.

Recursive partitioning was performed as an alternative technique using the data mining program, CART® [10]. Our experience suggests that recursive partitioning may be more suitable than logistic regression in certain clinical situations. This has also been found in the creation of other decision rules [11].

Recursive partitioning uses the technique of 'binary recursive partitioning' to create a decision tree. It is binary as it always splits parent nodes (or decision rules) into two child nodes. It is recursive as it then uses each child node as the parent node to create the next step in the tree. The tree is complete when further splitting produces no improvement in the predictive ability of the tree. Before commencing the analysis, we set a priori objectives of deriving a rule with a 50% sensitivity for prediction of prolonged ventilation.

2.5. Sample size

Although formal power calculations do not exist for creating a decision rule, a commonly used 'rule of thumb' is that there should be ten outcome events per independent variable in the prediction rule [12]. We feel that a rule with over ten variables is difficult to use and thus we required at least 100 patients with prolonged ventilation. The above timeframe of data collection was thus selected so that this figure would easily be achieved in both the derivation and validation datasets.

2.6. Ethics

Ethics committees were approached but full approval for this study was not required as all data was anonymised prior to analysis.

3. Results

The records of 3070 patients were analysed from the North Staffordshire Hospital Open Heart Registry. This contained 201 patients who were ventilated for over 24 h. The records of 3921 patients were then analysed from the Blackpool Victoria Hospital Open Heart Registry. This contained 124 patients who were ventilated for over 24 h. This was used only to assess the external validity of the derived rule. A descriptive analysis of both these databases is given in Table 1 and the time distributions of those ventilated longer than 6 h is shown in Fig. 1.

Univariate analysis on the North Staffordshire database found several factors that were significantly associated with

Table 1
Patient demographics

	North Staffordshire Database		Blackpool Victoria Database	
Number of patients	3070		3921	
Age (SD)	63	(9)	63	(9)
No. male	2331	76%	2889	74%
CABG only	2387	78%	3056	78%
CABG + valve	246	8.0%	325	8.3%
Valve	387	13%	471	12.0%
Other	50	1.6%	69	1.8%
Mean Parsonnet (SD)	7.0	(6.0)	7.6	(7.4)
No. of patients ventilated <12 h	659	21%	459	12%
No. of patients ventilated >24 h	201	6.5%	124	3.1%
No. of patients ventilated >48 h	156	5.1%	86	2.1%
No. of patients ventilated >4 days	130	4.2%	62	1.6%
No. of patients ventilated >7 days	85	2.8%	25	0.6%

prolonged ventilation (shown in Table 2). These were entered into the multivariate analysis.

After the two methods of multivariate analysis, it was found that the optimal rule was obtained by recursive partitioning (Fig. 2 and Table 3). This rule, when applied to the derivation dataset, correctly identifies 50% (100 patients) of those who went on to require prolonged ventilation, while only selecting 282 patients as high risk who did not need prolonged ventilation (negative predictive value of 96%). When tested on the Blackpool Victoria Database, the sensitivity was 52% and the negative predictive value was 98%, thus identifying 65 of the 124 patients who required prolonged ventilation (Table 3).

As we used Parsonnet as part of our decision rule, we looked to see whether a specific Parsonnet score could be found which identified 50% of those who went on to receive prolonged ventilation. A Parsonnet score of 10 identified 98 of the 201 patients (49%) in the North Staffordshire database who required prolonged ventilation. However, 618 patients who did not require prolonged ventilation also had a Parsonnet score of over 10 giving a specificity of only 78%.

A scoring system was also generated using logistic

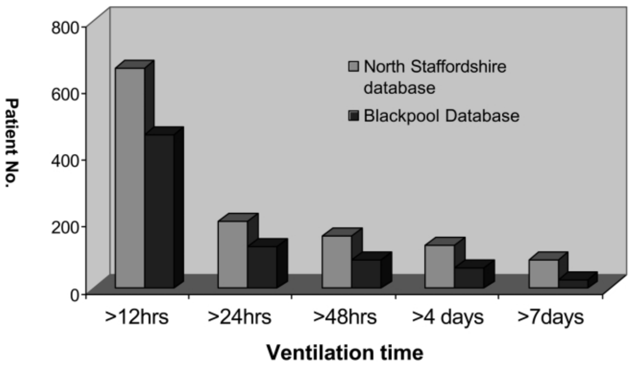

Fig. 1. Ventilation time for patients ventilated longer than 6 h.

1. Is the Parsonnet score under 7 ?
- If yes, patient is Low risk

If the Parsonnet score is 7 or more :
2. Is the LVEF poor ? - If yes, patient is high risk

3. If the age of the patient is over 65 is the PA systolic pressu over 35 ?
- If yes, patient is high risk

4. Patients having an Emergency re-operation for bleeding or cardiac arrest are all high risk.

If none of the above, consider patients to be low risk.

Fig. 2. Prolonged ventilation decision rule.

regression (Table 4 and Fig. 3). A simple summative scoring system was generated from the odds ratios of those variables that displayed a significant relationship with prolonged ventilation after multivariate analysis, in a method similar to that of the derivation of the Parsonnet score and the Euroscore [13,14]. This was done rather than generating a complex rule from the logistic equation, as we felt that the mathematically exact rules are not useful clinically.

The score of 13.5 was found to select 47% of those who had prolonged ventilation. However, there were 533 patients who did not need prolonged ventilation who had a score of over 13.5 and thus although the specificity of 81% was superior to using the Parsonnet score, the recursive partitioning decision rule was still superior to the logistic regression model.

Finally, a large number of patients cannot have the timings of their operation delayed and thus it is useful to know how our rule performs only in non-emergency situations. We excluded all patients having an emergency or

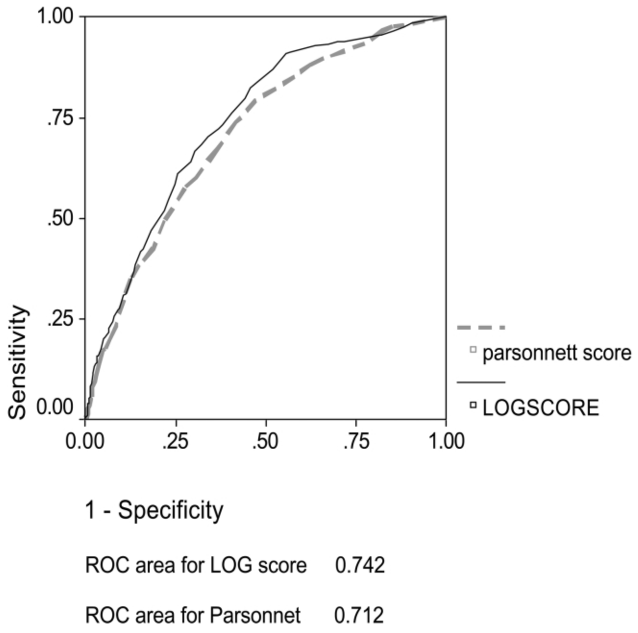

Fig. 3. ROC curve of LOG score and Parsonnet score.

Table 2
Univariate analysis of North Staffordshire database

	Ventilation <24 h		Ventilation >24 h		*P*-value
Number of patients	2869	94%	201	6.6%	
Age	62 years		67 years		<0.0005
Sex	2037	71%	153	76%	0.07
In-patient transfer	631	22%	78	39%	<0.0005
Diagnosis					
IHD	2453	86%	153	76%	0.017
AVD	238	8.3%	24	12%	
MVD	106	3.7%	14	6.8%	
Other	72	2.5%	10	5.2%	
Mean angina status (CCS)	2.5		2.4		0.277
Mean dyspnoea status (NYHA)	2.3		2.6		<0.0005
Hypertension	1402	49.0%	112	56%	0.064
Current Smoker	243	8.5%	14	7.0%	0.522
Hx of COPD	137	4.8%	20	10.0%	0.006
Atrial fibrillation	194	6.8%	32	16%	<0.0005
Prev CVA or TIA	255	8.9%	35	17%	<0.0005
IDDM	164	5.7%	13	6.5%	0.898
Mean BMI	28		28		0.118
Hypercholesterolemia	1806	64%	99	50%	<0.0005
Unstable symptoms	1348	47%	121	60%	<0.0005
LVF currently requiring diuretics	629	22%	95	48%	<0.0005
Absence of Prev ‘Q’ Mis	1660	59%	113	57%	0.270
Thrombolysis in last 24 h	34	1.2%	7	3.6%	0.006
Prev. cardiological intervention	234	8.2%	10	5.0%	0.113
Prev. cardiac surgery	172	6.0%	25	13%	<0.0005
Cr >200	18	0.6%	9	4.5%	<0.0005
Cath on this admission	455	16%	56	28%	<0.0005
LMS disease <50%	427	15%	30	15%	0.980
Mean PA systolic	5.72		15.8		<0.0005
LVEF					
Good	1924	67%	94	47%	<0.0005
Moderate	801	28%	77	38%	
Poor	143	5.0%	30	15%	
Pacemaker	23	0.8%	4	2%	0.08
IV nitrates until op	197	6.9%	38	19%	<0.0005
Cardiogenic Shock	30	1.0%	18	9.0%	<0.0005
IV inotropes pre-op	28	1.0%	16	8.0%	<0.0005
Emergency operation	109	3.8%	32	16%	<0.0005
Mean Parsonnet Score	6.7		11.4		<0.0005
Simple Bayes score	2.2		5.5		<0.0005
Complex Bayes score	1.9		6.0		<0.0005

Table 3
Performance of prolonged ventilation decision rule

Predicted risk by decision rule	Total cases	Ventilation >24 h	Ventilation <24 h
North Staffordshire open heart registry			
Total cases	3070	201	2869
High Risk	382	100	282
Low Risk	2688	101	2587
Sensitivity		50%	43–57%
Specificity		90%	89–91%
Blackpool Victoria Open Heart Registry			
Total cases	3921	124	3797
High risk	438	65	373
Low risk	3483	59	3424
Sensitivity		52%	44–62%
Specificity		90%	89–91%

Table 4
Logistic Regression scoring for prediction of prolonged ventilation

	Odds ratio	Significance	Weight allocated
Current diuretic use for LVF	1.8	0.001	2
Poor ejection fraction	2.5	0.001	2.5
IV nitrates until operation	2.9	<0.0005	3
Parsonnet increment of 1	1.0	<0.0005	1 per point
Age over 65	1.6	0.012	1.5
Creatinine over 200	3.3	<0.0005	3
Redo operation	1.7	0.032	1.5
Results of logistic rule in the North Staffordshire Dataset	Ventilation >24 h	Ventilation <24 h	
High risk score (>13.5)	95	533	
Low risk score(≤13.5)	106	2336	
Sensitivity	47%	40–54%	
Specificity	81%	80–83%	
Results of logistic rule in the Blackpool Dataset			
High risk score (>13.5)	70	773	
Low risk score(≤13.5)	54	3024	
Sensitivity	56%	47–65%	
Specificity	80%	78–81%	

salvage operation and all those that required an emergency re-operation. This removed 335 patients from the North Staffordshire Database of whom 85 required prolonged ventilation. It also further simplified our decision rule, by removing the last criterion.

The results are shown in Table 5. While the sensitivity was reduced to 30%, the specificity increased to 93%, and therefore only 206 patients are selected as high risk patients using this rule. The rule's performance is maintained in the Blackpool database when these patient exclusions are repeated and rule again outperforms the Parsonnet rule alone.

4. Discussion

We have derived and validated a decision rule that successfully predicts half of those patients who go on to require prolonged ventilation. More importantly only 9.8% of those who do not require prolonged ventilation are misclassified by our rule. This rule outperforms the use of the Parsonnet score alone as a predictor and the best available rule that we were able to derive by logistic regression.

Our decision rule classifies 14% of all cardiac patients as high risk which we feel is highly useful clinically. In units that do not operate at the same rate during the weekend, there is often some spare capacity by the Sunday in the Intensive care unit. If a protocol was initiated in departments whereby patients identified as high risk were listed for Friday operating, then 50% of all those requiring prolonged ventilation would be initially cared for over the weekend. This would reduce the likelihood that beds would be unavailable for the next days operating.

Table 5
Performance of decision rule if all patients having an emergency or salvage operation or patients that require reoperation for bleeding or cardiac arrest, are excluded

Predicted risk by decision rule	Total cases	Ventilation >24 h	Ventilation <24 h
North Staffordshire open heart registry			
Total cases	2735	116	2619
High risk	206	35	171
Low risk	2529	81	2448
Sensitivity		30%	22–39%
Specificity		93%	93–94%
Blackpool Victoria Open Heart Registry			
Total cases	2783	61	2722
High risk	200	19	181
Low risk	2583	42	2541
Sensitivity		31%	20–44%
Specificity		93%	98–99%

Additionally, if there was a situation in the Intensive care where there was a period of particular pressure on beds, then delaying surgery on patients identified by us as high risk by our rule would halve the likelihood of adding a patient to the intensive care who will go on to receive prolonged ventilation.

This analysis has weaknesses. Our outcome variable of ventilation for over 24 h was accurately and consistently recorded and this is constantly monitored in our units. But the decision to extubate was left to local protocols at the two institutions or the decision making of clinicians caring for the patient. Although many patients will clearly be unable to be extubated at 24 h, there will be situations where a more aggressive extubation policy will lead to earlier extubation. This may account for the difference in incidence of patients extubated at 24 h in North Staffordshire and in Blackpool. An alternative outcome measure would have been the number of hours to achieve a set arterial oxygen partial pressure for given ventilator parameters, but we felt that this would not make the interpretation of our results easier for clinicians assessing this decision rule. Indeed by validating our rule in a unit with a different rate of prolonged ventilation, we have shown that our rule is robust to differing policies of extubation.

Our dataset does not include data on pulmonary function testing for our patients. However, Jacob et al. [15] in a cohort of 193 patients found that pulmonary function tests do not predict length of mechanical ventilation, incidence of pleural effusions or incidence of pulmonary oedema, and thus we do not think that this is a major weakness of our study.

Our decision rule identifies patients having an emergency re-operation as high risk. While these patients can clearly not have their operation times modified when using our rule to plan operative timings, we wanted to provide a decision rule that was applicable to all patients in the database. For this reason, we did not initially exclude these patients from the analysis. However, the performance of our rule also performed well when emergency patients were excluded. It should be noted that the performance of the Parsonnet score and the logistic score also deteriorates when these patients are excluded and thus our decision rule is still the optimal rule for high risk prediction.

There are well established standards for the development of clinical decision rules [16]. We have fulfilled standards required for the derivation and validation of a clinical decision rule prior to implementation, although there are several areas of further analysis that could be performed for this rule. It is recommended that each variable and the rule as a whole is assessed for inter-observer agreement. We feel that each category in our rule is has a high reliability and reproducibility, and thus we hope that different clinicians will categorise patients as high or low risk using our rule with a high degree of accuracy. We do, however, need to establish this in future studies. We also intend to investigate whether the implementation of this rule in a busy CSU can actually reduce the rate of cancelled operations in busy UK CSUs.

Our findings of preoperative clinical factors that predict prolonged ventilation agree with other studies. Branca et al. [3] identified mortality risk scoring to be the most correlated factor with prolonged ventilation, and also that only age and operative urgency could be added to this to improve its predictive ability. They did not, however, validate any recommendations for high risk patient identification. A smaller study by Spivack et al. [6] found only ejection fraction to be related to prolonged ventilation. Higgins et al. [4] derived and validated a scoring system to predict either mortality or any intensive care morbidity including prolonged ventilation. Their scoring system included severe left ventricular dysfunction, age over 65 years, and emergency operation as significant predictors for prolonged ventilation. However, this scoring system includes intra-operative factors as it was designed to assess intensive care treatment, and is thus of little use to clinicians wanting to risk-stratify patients pre-operatively.

5. Conclusion

Our clinical decision rule is the first validated rule that identifies patients at high risk of prolonged ventilation. We identify 14% of all cardiac patients with this rule, but 50% of patients that require prolonged ventilation are included in this cohort. This outperforms any other current risk stratification systems including established mortality scores, and we thus recommend this rule for better planning of high risk patients in the context of limited intensive care resources.

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