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Prediction of Prolonged Ventilation after Coronary Artery Bypass Grafting: Data from an Artificial Neural Network

Eric S. Wise, MD,[1] David P. Stonko, MS,[2] Zachary A. Glaser, BA,[2] Kelly L. Garcia, MD,[2] Jennifer J. Huang, BA,[2] Justine S. Kim, BS,[2] Justiss A. Kallos, MS,[2] Joseph R. Starnes, BA,[2] Jacob W. Fleming, BS,[2] Kyle M. Hocking, PhD,[1] Colleen M. Brophy, MD,[3,1] Susan S. Eagle, MD[4]

[1]Department of Surgery, Vanderbilt University, Nashville, TN; [2]Vanderbilt University School of Medicine, Nashville, TN; [3]Department of Surgery, Tennessee Valley Healthcare System, Nashville, TN; [4]Department of Anesthesiology, Vanderbilt University; Division of Cardiothoracic Anesthesiology, Nashville, TN

ABSTRACT

Objectives: The need for mechanical ventilation 24 hours after coronary artery bypass grafting (CABG) is considered a morbidity by the Society of Thoracic Surgeons. The purpose of this investigation was twofold: to identify simple preoperative patient factors independently associated with prolonged ventilation and to optimize prediction and early identification of patients prone to prolonged ventilation using an artificial neural network (ANN).

Methods: Using the institutional Adult Cardiac Database, 738 patients who underwent CABG since 2005 were reviewed for preoperative factors independently associated with prolonged postoperative ventilation. Prediction of prolonged ventilation from the identified variables was modeled using both "traditional" multiple logistic regression and an ANN. The two models were compared using Pearson r^2 and area under the curve (AUC) parameters.

Results: Of 738 included patients, 14% (104/738) required mechanical ventilation ≥ 24 hours postoperatively. Upon multivariate analysis, higher body-mass index (BMI; odds ratio [OR] 1.10 per unit, $P < 0.001$), lower ejection fraction (OR 0.97 per %, $P = 0.01$) and use of cardiopulmonary bypass (OR 2.59, $P = 0.02$) were independently predictive of prolonged ventilation. The Pearson r^2 and AUC of the multivariate nominal logistic regression model were 0.086 and 0.698 ± 0.05, respectively; analogous statistics of the ANN model were 0.159 and 0.732 ± 0.05, respectively.

BMI, ejection fraction and cardiopulmonary bypass represent three simple factors that may predict prolonged ventilation after CABG. Early identification of these patients can be optimized using an ANN, an emerging paradigm for clinical outcomes modeling that may consider complex relationships among these variables.

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Correspondence: Eric S Wise, MD, Department of Surgery, Vanderbilt University, Nashville, TN 37232; 314-374-0354 (preferred) or 615-322-5198; fax: 615-936-5988 (e-mail: ericstephenwise@gmail.com).

INTRODUCTION

Since its inception in 1989, the Society of Thoracic Surgeons (STS) National Adult Cardiac Surgery Database has sought to be a comprehensive resource in outcomes after coronary artery bypass grafting (CABG). The database has over five million records of cardiac surgical operations since 1990, which reflect the populations of over one thousand unique institutions [Shahian 2007; Jacobs 2013]. Through the establishment of the Quality Measurement Task Force, the STS has also developed a Composite Quality Score consisting of eleven outcome measures within four domains [O'Brien 2007]. These domains are operative care, perioperative medical care, risk-adjusted mortality and risk-adjusted major morbidity. Each of these measures has been endorsed by the National Quality Forum [O'Brien 2007; Shahian 2007; Jacobs 2013].

Prompt extubation is one such measure of surgical quality, and prolonged ventilation, defined as greater than 24 hours after CABG, is considered a major morbidity [O'Brien 2007]. Increasingly, patients undergoing CABG are being extubated within six hours after surgery [Camp 2009]. It is the practice of several institutions to extubate in the operating room, particularly for patients who did not require cardiopulmonary bypass. Early extubation has been successful, with very low rates of postoperative cardiorespiratory complications and reintubation [Lobdell 2009; Dorsa 2011; Blanco 2012]. However, it is accepted that a subset of patients will likely require at least twenty-four hours before extubation due to myriad preoperative, intraoperative and postoperative factors [Hawkes 2003; Siddiqui 2012]. Not only is the prediction of those patients who may require prolonged ventilation important at the patient-level, but it is critical for proper context and risk-adjustment in systems-level outcome analyses in the assessment of quality of care. To date, multiple studies have identified a panel of preoperative risk factors for prolonged ventilation [London 1998; Rady 1999; Cislaghi 2009; Ji 2010; Dorsa 2011; Blanco 2012; Ji 2012; Saleh 2012; Shahbazi 2012; Siddiqui 2012; Totonchi 2014].

An artificial neural network (ANN) is a computational construct in which a model is "taught" to predict an outcome based on input variables through pattern recognition [Penny

1996]. Using a series of training nodes, the model develops a robust algorithm and ultimately outputs a prediction. Its use as a tool for surgical diagnostic and prognostic modeling is emerging. Its benefits lie in its ability to continually adapt to newly input patient data, internal validity, less ambiguous predictions and higher discriminant ability relative to analogous models derived from traditional multiple regression [Yoldas 2012; Cruz-Ramirez 2015; Wise 2015]. In this investigation, we first aim to determine the most important simple and easily available preoperative risk factors for prolonged ventilation. Considering these risk factors, we further aim to employ ANN modeling to optimize the prediction of prolonged ventilation, and to contrast with a traditional multiple logistic regression model.

MATERIALS AND METHODS:

Anesthetic, operative and extubation protocols

All patients undergoing CABG were induced with intravenous fentanyl, propofol, midazolam, and rocuronium. They were subsequently intubated, mechanically ventilated, and received general anesthesia with 0.7 to 1 minimum alveolar concentration isoflurane throughout the case. Patients received standard and invasive hemodynamic monitors, including an intra-arterial catheter for continuous blood pressure measurements, central venous access with a 9-French catheter, and a pulmonary artery catheter for pulmonary arterial and central venous pressure measurements. Patients were prepped and draped in sterile fashion for sternotomy and saphenous vein graft harvest. The decision to initiate cardiopulmonary bypass was based on hemodynamic stability, size of target coronary arteries, and surgeon preference. Patients who received cardiopulmonary bypass had central aortic cannulation and a single stage venous cannula placed in the right atrium.

A select group received pump-assist decompression of the ventricle without aortic cross-clamp or cardioplegia. The remainder received an aortic cross-clamp and underwent full arrest with antegrade cardioplegia. Both cardiopulmonary bypass groups remained at a temperature between 32 and 34 degrees Celsius.

Following surgery isoflurane was discontinued and all patients were transported intubated with hand-assist ventilation to the cardiovascular intensive care unit (CVICU). General anesthesia was maintained with a propofol infusion. Upon arrival to the CVICU, propofol was continued for four additional hours, and the residual neuromuscular blockade was fully reversed within the first hour. A standard CVICU ventilator protocol was implemented for all patients following CABG. Postoperative mechanical ventilation was achieved with pressure regulated volume control with synchronized intermittent mandatory ventilation and tidal volume of 7-8 ml/kg ideal body weight. Adjusting the tidal volume to as low as 4-5 ml/kg was accepted to maintain plateau pressures less than 30 cm H_2O. Respiratory rate was adjusted to maintain PCO_2 < 55 mmHg with an arterial pH 7.32-7.42. Initial positive end-expiratory pressure (PEEP) was set at 8 cm H_2O in an effort to increase surface area for gas exchange.

Patients were assessed for ventilator weaning after four hours by the staff attending and nurse practitioners. Per protocol, extubation criteria included hemodynamic stability with minimal inotropic support, body temperature > 36.5°C, and chest tube blood output < 100 mL/hr. Propofol was titrated down for initiation of spontaneous ventilation. At this point, ventilation mode was switched to pressure support by respiratory therapy staff, which was titrated to maintain a tidal volume of a least 5-6 mL/kg ideal body weight. FiO_2 was decreased with a goal of FiO_2 of 0.40, and a PEEP of 5 mmHg while maintaining SpO_2 > 94%. CVICU staff physicians, nurse practitioners, nursing staff, and respiratory therapy were all present for discontinuation of mechanical ventilation and extubation.

Patient selection

This was a retrospective, single-institution study conducted using the Vanderbilt University Synthetic Derivative, a de-identified patient database that mirrors StarPanel, the electronic medical record system [Roden 2008]. As no patient identifiers are available in this database, the Vanderbilt University Institutional Review Board granted approval with waived informed consent. The Synthetic Derivative contains the institutional STS database registry with data primarily logged since 2005, and cardiac surgical patient cohorts can be separated by length of ventilation. The initial search criterion for patients who underwent CABG, as indicated by Current Procedural Terminology (CPT) code attribution (33517-33519, 33521-33523, 33514, 33516, 33533-33536), identified 168 CABG patients requiring, and 751 CABG patients not requiring prolonged ventilation, for a total of 919 patients. Patients were excluded for operation who received CABG outside of the study timeframe (n = 9). Additional exclusion criteria include the performance of a concomitant major operation (ie, valve replacement or repair, carotid endarterectomy; n = 146), intubation prior to CABG (n = 8), re-intubation

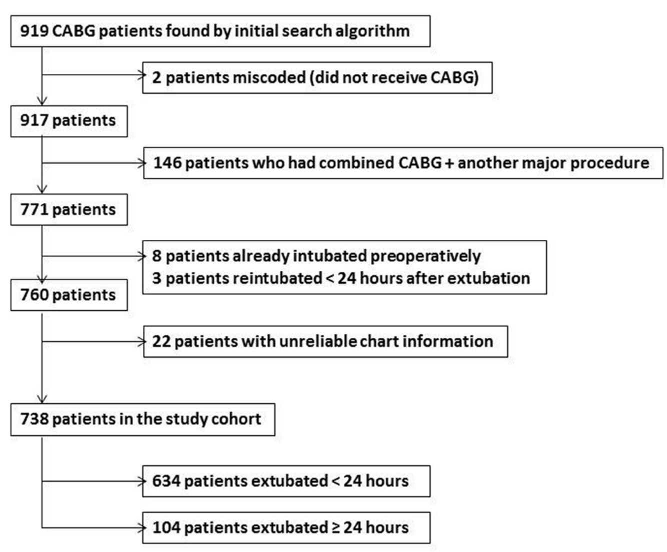

Figure 1. Derivation of the 738 patient study cohort.

required within 24 hours (n = 3) or insufficient information in the medical record (n = 22). Derivation of the cohort is illustrated in Figure 1. Ultimately, 738 patients were included for analysis.

Data collection and analysis

Included patients underwent directed chart review for select simple preoperative factors including baseline demographics and measures that have previously been associated with prolonged ventilation. Baseline demographics included gender, age, race, and body-mass index (BMI) [London 1998; Cislaghi 2009; Ji 2012; Saleh 2012; Shahbazi 2012]. Additionally, diagnosis of chronic obstructive pulmonary disease was considered [Cislaghi 2009; Siddiqui 2012]. Previously validated laboratory studies examined included baseline arterial oxygen tension, packed cell volume, glycated hemoglobin (as a surrogate for blood glucose control), measures of renal function (urea nitrogen and creatinine) and platelet count [Dorsa 2011]. Home medications that may plausibly influence prolonged ventilation were reviewed. Ejection fraction, smoking history, inpatient status, use of cardiopulmonary bypass and number of target vessels were included as well [Cislaghi 2007; Cislaghi 2009; Blanco 2012; Siddiqui 2012]. Differences in each of these variables between the two cohorts were compared using the Mann-Whitney U test or Fisher's exact test as appropriate. Variables differing at a trend level ($P \leq 0.1$) on bivariate analysis were input into a forward stepwise multivariate nominal logistic regression analysis to assess for independent association ($P \leq 0.05$) with prolonged ventilation. Independent predictors of prolonged ventilation were used to create predictive models by derivation of a multiple logistic regression expression and imputation into a multivariable ANN.

In brief, ANN variables are input, with 80% of patients randomly selected to comprise a training set to generate a prediction algorithm. The remaining 20% are withheld to ensure internal validation. The learned model outputs a

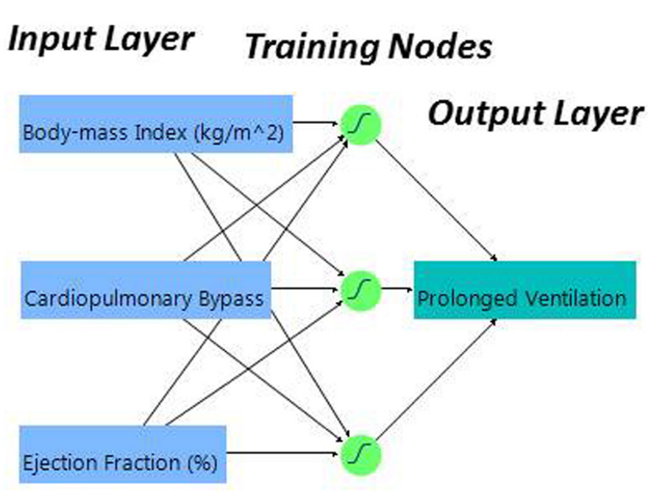

Figure 2. Schematic of the three-variable, three-node artificial neural network model for the optimized prediction of prolonged ventilation.

Table 1. Bivariate analysis of postoperatively variables correlated with prolonged ventilation.

Preoperative Variable	Extubation < 24 hours (n = 634)	Prolonged ventilation* (n = 104)	*P*
Demographics			
Male gender	72% (454/634)	65% (68/104)	.20
Black race	6% (36/608)	3% (3/94)	.46
Age (years)	62.6 (55.5-71.1) (n = 634)	63.9 (58.1-71.5) (n = 104)	.26
Body Mass Index (kg/m^2)	29.1 (25.8-33.5) (n = 308)	33.9 (27.8-40.8) (n = 42)	<.001
COPD	6% (35/634)	8% (8/104)	.37
Preoperative laboratory studies			
White blood cell count ($\times 10^6$/mL)	7.3 (6.2-9.0) (n = 625)	8.0 (6.5-10.1) (n = 104)	.01
Packed cell volume (%)	41 (37-44)(n = 629)	40 (35-43)(n = 104)	.06
Platelet count ($\times 10^6$/mL)	211 (176-253) (n = 627)	216 (175-266) (n = 104)	.29
Urea nitrogen (mg/dL)	15 (11-20)(n = 622)	17 (12-24)(n = 101)	.004
Creatinine (mg/dL)	0.97 (0.80-1.12) (n = 621)	1.00 (0.83-1.26) (n = 101)	.09
HgbA1c (%)	6.1 (5.7-7.1) (n = 589)	6.4 (5.9-7.3) (n = 85)	.04
PaO_2 (mm Hg)	79 (71-91)(n = 229)	74 (67-82)(n = 33)	.006
Home Medications			
Aspirin	55% (349/634)	42% (41/97)	.02
Clopidogrel	21% (122/592)	20% (19/97)	.89
Beta blocker	46% (271/592)	40% (39/97)	.32
Calcium channel blocker	21% (126/592)	9% (9/97)	.005
Nitrate	23% (138/592)	21% (20/97)	.60
Statin	51% (299/592)	39% (38/97)	.05
Diuretics	31% (183/592)	25% (24/97)	.23
ACE inhibitor or ARB[2]	54% (320/592)	38% (37/97)	.004
Additional Factors			
Inpatient status	73% (462/631)	78% (80/102)	.33
Current smoker	36% (220/614)	37% (37/100)	.82
Ever Smoker	65% (396/614)	60% (60/100)	.43
Ejection fraction (%)	55 (45-60)(n = 579)	50 (35-55)(n = 98)	<.001
Use of cardiopulmonary bypass	56% (351/632)	79% (75/95)	<.001
Number of vessels	3 (2-3)(n = 633)	3 (2-3)(n = 104)	.65

P values obtained via Mann-Whitney U test or Fisher's exact test, as appropriate.
*Prolonged ventilation: ≥24 hours
†ACE, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker

score between 0 (lowest probability) and 1 (highest probability), reflecting the probability of prolonged ventilation [Wise 2015]. To prevent over-fitting the data, a back-propagation ANN with *k*-fold validation was used. Three nodes, each assigned a learning value of 0.333 were used, and the model was trained with three iterations. The full mathematical description of ANN methodology has been previously reviewed [Piaggi 2010; Dumont 2011]. A schematic representation of the ANN model is illustrated in Figure 2. Actual versus predicted outcome plots, as well as receiver-operating characteristic (ROC) curves were generated for both models, using Pearson r^2 and area under the curve (AUC, expressed as AUC ± standard error)[Cook 2007] as primary measures of each model's discriminant ability [Wise 2015].

Bivariate and multivariate analysis was performed using GraphPad Prism 5 (La Jolla, CA) and JMP Pro 11 (Cary, NC). Graphical generation was performed using GraphPad Prism 5, and ANN modeling was performed using JMP Pro 11. Measures of central tendency were reported as median (interquartile range). The level of evidence used to denote statistical significance was $P \leq 0.05$.

RESULTS

The study population totaled 738 evaluable CABG patients. Of the 738 patients, 71% were male, 6% were black, the median age was 62.8 (56.0-71.1) years and median BMI was 29.5 (25.8-34.4) kg/m^2. The baseline patient demographics and characteristics, contrasted in bivariate fashion between the two patient cohorts, are reported in Table 1.

Differences (at $P \leq 0.1$) between the two groups were found for 12 variables, including BMI ($P < 0.001$), white blood cell count ($P = 0.01$), packed cell volume ($P = 0.06$), urea nitrogen ($P = 0.004$), creatinine ($P = 0.09$), glycated hemoglobin ($P = 0.04$), arterial oxygen partial pressure ($P = 0.006$), aspirin use ($P = 0.02$), calcium channel blocker use ($P = 0.005$), statin use ($P = 0.05$), angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use ($P = 0.004$), ejection fraction ($P < 0.001$) and use of cardiopulmonary bypass ($P < 0.001$).

Subsequent multivariate analysis was performed. Independent preoperative predictors of prolonged ventilation after CABG included higher BMI (odds ratio 1.10 per unit BMI, $P < 0.001$), depressed ejection fraction (odds ratio 0.97 per percent ejection fraction, $P = 0.01$) and use of cardiopulmonary bypass (odds ratio 2.59, $P = 0.02$). Full results of the multivariate analysis are reported in Table 2.

Considering the variables BMI, ejection fraction and use of cardiopulmonary bypass, a multiple logistic regression expression was derived and the ANN model was created. Actual versus predicted outcome plots for both models are shown in Figure 3.

The Pearson r^2 values of the multiple logistic regression and ANN models were 0.086 and 0.159. Prediction of prolonged ventilation for both models was also assessed via ROC curve generation, seen in Figure 4. The AUC values for the multiple logistic regression, ANN training set and ANN validation set ROC curves were 0.698, 0.732 and 0.714, respectively. The ANN ROC curve was significantly more discriminant than that obtained from the multiple logistic regression model.

Table 2. Forward stepwise multivariate nominal logistic regression analysis for independent predictors of prolonged extubation.

Preoperative Variable	OR (95% CI)	*P*
Body Mass Index (kg/m^2)	1.10 (1.05, 1.16)	<.001
White blood cell count (x106/mL)	1.06 (0.94, 1.16)	.28
Packed cell volume (%)	0.94 (0.88, 1.01)	.08
Urea nitrogen (mg/dL)	-	-
Creatinine (mg/dL)	-	-
HgbA1c (%)	-	-
PaO_2 (mm Hg)	-	-
Aspirin	0.86 (0.41, 1.83)	.69
Calcium channel blocker	-	-
Statin	-	-
ACE inhibitor or ARB*	-	-
Ejection fraction	0.97 (0.94, 0.99)	.01
Use of cardiopulmonary bypass	2.59 (1.21, 5.97)	.02

$n = 330$, $r^2 = .13$, Chi square = 30.6, $P < 0.001$.

Dashes indicate variable was dropped upon stepwise regression. Odds ratios expressed per unit increase in regressor.

*ACE, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker

DISCUSSION

Timely extubation after CABG is important, as it may lead to more rapid recovery, shorter intensive care requirements, and reduced costs of hospitalization. The STS has defined prolonged ventilation as an excess of 24 hours postoperatively. Variance in length of mechanical ventilation is primarily governed by preoperative patient factors [Saleh 2012]. As such, our study identified three key independent risk factors for prolonged ventilation, and sought to optimize the ability to predict prolonged ventilation using an ANN model.

Within our cohort we found that higher BMI, depressed ejection fraction, and use of cardiopulmonary bypass were associated with prolonged ventilation after CABG. The association of elevated BMI and prolonged ventilation has been demonstrated in other studies [Kuduvalli 2002; Murthy 2007; Perrotta 2007], and most recently, by Saleh et al. in 2012, in which patients with a BMI > 35 kg/m^2 had a significantly increased risk of ventilation requirement of greater than 72 hours [Saleh 2012]. This finding is likely due to impaired chest wall mechanics of respiration, leading to difficulty in gas exchange and subsequent delay in meeting extubation parameters [Leme Silva 2012]. Additionally, obese patients have greater airway inflammation and hyper-responsiveness at baseline, and may require more sophisticated ventilator

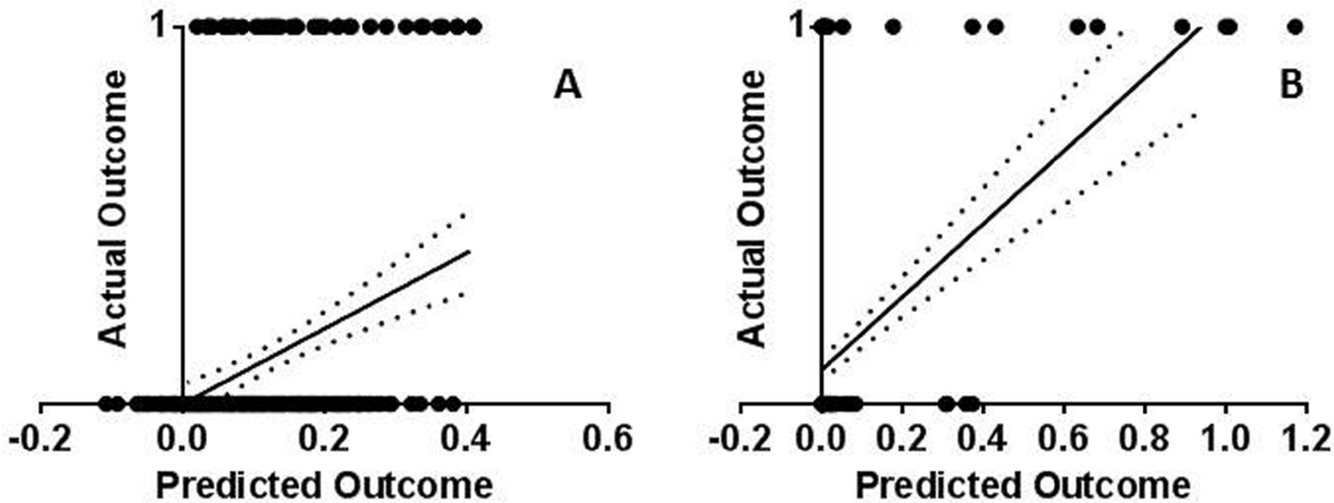

Figure 3. Actual versus Predicted outcome scatterplots for prediction of prolonged ventilation
A. Multiple logistic regression: n = 331, r^2 = .086; B. Artificial neural network training set algorithm (applied to patients from both training and validation sets): n = 331, r^2 = .159.
0 reflects rapid extubation, 1 reflects prolonged ventilation (≥ 24 hours postoperatively). Simple linear regression lines shown with 95% confidence band.

management leading up to extubation [Leme Silva 2012]. This finding could also be due to the association of elevated BMI with a lengthier, more difficult operation.

Depressed ejection fraction has been validated as a predictor of prolonged ventilation after CABG. Cislaghi et al. and Blanco et al. found that a preoperative ejection fraction of 30% or less conferred increased risks of ventilation beyond twelve hours and inability to extubate in the operating room following a CABG procedure, respectively [Cislaghi 2009; Blanco 2012]. An imperfect clinical surrogate for depressed ejection fraction, preoperative congestive heart failure, was found to be a risk factor for ventilator dependency in a Chinese cohort [Ji 2012]. Mild pulmonary edema is very common in CABG patients, particularly those who required cardiopulmonary bypass [Cislaghi 2009]. Ji et al. argued that patients with congestive heart failure were more likely to have postoperative hypoxemia, perhaps due to more severe pre-existing pulmonary interstitial edema [Ji 2012]. In our analysis, ejection fraction was considered as a continuous variable, and was shown to independently and inversely predict prolonged ventilation after CABG.

Prospective randomized trials have failed to demonstrate a benefit to off-pump CABG with respect to short-term rates of death, myocardial infarction, stroke, or new renal failure [Lamy 2012; Moller 2012; Lamy 2013]. However, several benefits to off-pump surgery include improved organ protection [Sepehripour 2014], reduced postoperative stroke [Sa 2012; Vasques 2013], and reduced postoperative atrial fibrillation [Moller 2008]. Cardiopulmonary bypass can generate a systemic inflammatory response, cause reperfusion injury upon cessation, and promote generation of reactive oxygen species [Ji 2010; Huffmyer 2015]. As such, one additional benefit of off-pump CABG is a decreased ventilation requirement. In the cohorts of Cislaghi et al. and Ji et al., cardiopulmonary bypass time was found to be in direct proportion to prolonged ventilation requirements [Cislaghi 2009; Ji 2010]. Non-use of cardiopulmonary bypass also predicted successful extubation in the operating room [Blanco 2012]. Our data, in parallel with prior studies, implicate the use of cardiopulmonary bypass as an independent risk factor for prolonged ventilation.

Our data did not detect the association of several key factors with prolonged ventilation – notably, advanced age. Advanced age is an established predictor of both prolonged ventilation and extubation failure in a diverse series of cohorts, particularly in those over the age of 65 [London 1998; Rady 1999; Cislaghi 2009; Saleh 2012; Shahbazi 2012]. Arterial oxygen tension on room air is routinely obtained during preoperative assessment if feasible. A low value may suggest chronic obstructive pulmonary disease or poor cardiopulmonary reserve, pathologies that may be exacerbated immediately postoperatively and during the period of ventilator weaning [Ji 2010; Siddiqui 2012]. Similarly, anemia and renal impairment have also been shown to predict ventilator dependency [Rady 1999; Cislaghi 2009; Dorsa 2011; Ji 2012; Saleh 2012; Siddiqui 2012; Totonchi 2014]. In our study, arterial oxygen tension, anemia (packed cell volume), and renal function (blood urea nitrogen) were all correlated with prolonged ventilation, although these metrics lost independent significance upon multivariate analysis.

The three identified independent predictors were modeled in two different ways. Traditional multiple logistic regression assigns a weight for each input variable and outputs a score that corresponds to the likelihood of an event – in this instance, prolonged ventilation. Ostensibly, determination of prolonged ventilation is more nuanced, and imputation of these variables in the ANN allows for improved recognition of the patterns and interactions among variables. In our study, the ANN algorithm, while far more complex, generated an

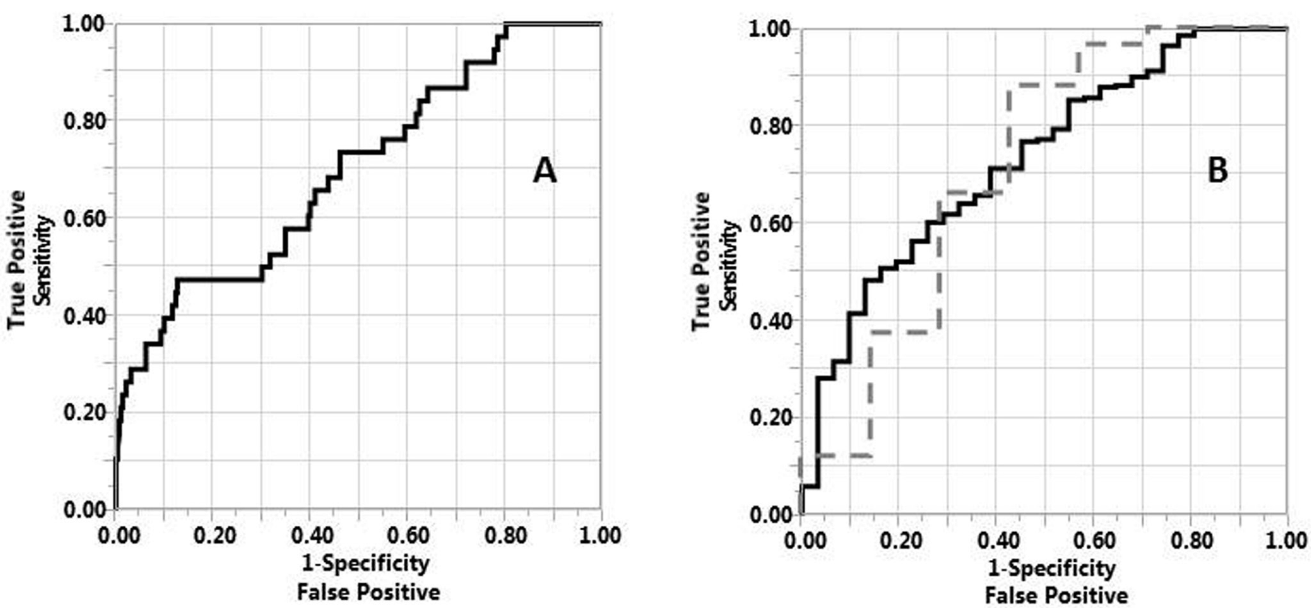

Figure 4. Receiver operating characteristic curves for prediction of prolonged ventilation
A. Multiple logistic regression algorithm: n = 331, AUC = .698. B. Artificial neural network training set algorithm: solid line reflects training set (n = 265, AUC = .732), dashed line reflects validation set (n = 66, AUC = .714).

internally validated predictive model that was superior to that derived by multiple logistic regression as characterized by the Pearson r^2 value and AUC. Despite its sophistication, ANN algorithms are well suited for use in generation of a widely available online based risk estimator, or for programming as a platform within an electronic medical record [Wise 2015]. The algorithm may also evolve and gain predictive power as further data is collected and input into the model.

Though the use of ANN in clinical medicine is thus far limited, it holds promise as a powerful prognostic tool. The current applications include assistance in the accurate diagnosis of acute appendicitis, detection of cervical cancer, and prediction of vasospasm after subarachnoid hemorrhage [Koss 1994; Prabhudesai 2008; Dumont 2011; Yoldas 2012]. ANN provides less ambiguous likelihood predictions for binary outcomes; as such, a well-validated ANN model is inimitably suited to the surgical field, particularly in determining futility of surgery preoperatively [Wise 2015]. In this study, as demonstrated by improved descriptive statistics of the ANN model, this methodology is uniquely suited to model the complex relationship among BMI, ejection fraction, and use of CPB to optimize the prediction of prolonged ventilation.

While revealing, our study was subject to limitations, primarily the considerable selection bias inherent in retrospective data collection and lack of external validation, as only patients representing the demographics and perioperative protocols within a single institution were considered. This ANN algorithm would certainly benefit from validation using national STS database information or from data from other high-volume institutions. Camp et al. report that extubation within nine hours postoperatively was the optimal cut-off for improved postoperative outcomes. Our use of 24 hours, while influenced by STS guidelines, may not, therefore, constitute the best measure of prolonged ventilation [Camp 2009]. Next, this model only considered the contribution of preoperative factors in predicting prolonged ventilation, ignoring the variance to the outcome contributed by intraoperative and postoperative factors. All patients were largely afforded similar perioperative treatment. However, the preferences, experience and abilities among providers were not uniform, a drawback inherent to most previous studies as well [London 1998]. Moreover, preoperative complexity of coronary artery disease pathology using a standardized assessment (eg, SYNTAX score) was not utilized, as the detailed pathology of coronary disease required was not available within the de-identified database; rather, only the number of vessels intervened upon was considered. Finally, while short-term repercussions are well characterized, the impact of prolonged ventilation after discharge remains to be fully appreciated. However, improved survival up to sixteen months postoperatively has been associated with prompt extubation [London 1998; O'Brien 2007; Camp 2009; Lobdell 2012; Saleh 2012; Shahbazi 2012].

CONCLUSION

Despite the limitations, our data reveal the association of high BMI, low ejection fraction, and use of cardiopulmonary bypass with prolonged ventilation after CABG. Using these variables to optimize prediction of prolonged ventilation can be improved by use of an ANN, providing optimal perioperative prognostic guidance for patients and the clinical care team.

AUTHOR CONTRIBUTIONS

Eric S. Wise participated in conception/design, data analysis/interpretation, drafting and critical revision, and statistical analysis. David P. Stonko and Zachary A. Glaser participated in drafting and critical revision of the article, as well as data collection. Kelly L. Garcia, Jennifer J. Huang, Justine S. Kim, Justiss A. Kallos, Joseph R. Starnes and Jacob W. Fleming participated in data collection. Kyle M. Hocking participated in drafting and critical revision of the article, and statistical analysis. Colleen M. Brophy participated in conception/design, data analysis/interpretation and assisted overseeing the project in its entirety. Susan S. Eagle participated in conception/design, data analysis/interpretation, drafting and critical revision and was responsible for overseeing all aspects of the project. All authors gave final approval of the manuscript.

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