

## Predicting intensive care unit-acquired weakness: A multilayer perceptron neural network approach

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### Abstract

In this editorial, we comment on the article by Wang and Long, published in a recent issue of the *World Journal of Clinical Cases*. The article addresses the challenge of predicting intensive care unit-acquired weakness (ICUAW), a neuromuscular disorder affecting critically ill patients, by employing a novel processing strategy based on repeated machine learning. The editorial presents a dataset comprising clinical, demographic, and laboratory variables from intensive care unit (ICU) patients and employs a multilayer perceptron neural network model to predict ICUAW. The authors also performed a feature importance analysis to identify the most relevant risk factors for ICUAW. This editorial contributes to the growing body of literature on predictive modeling in critical care, offering insights into the potential of machine learning approaches to improve patient outcomes and guide clinical decision-making in the ICU setting.

**Key Words:** Intensive care units; Intensive care unit-acquired weakness; Risk factors; Machine learning; Computer neural network

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**Core Tip:** Predicting intensive care unit-acquired weakness (ICUAW) is crucial for improving patient outcomes. This editorial presents the potential of machine learning, specifically the multilayer perceptron neural network model, in predicting ICUAW. Insights into ICUAW risk factors and guides clinical decision-making in critical care are offered. The importance of developing accurate and reliable predictive models to improve patient outcomes in the intensive care unit setting is also emphasized.

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## INTRODUCTION

Intensive care unit-acquired weakness (ICUAW) is a neuromuscular disorder that affects patients who have been admitted to an intensive care unit (ICU) for an extended period[1]. It is characterized by a generalized weakness that can affect both the respiratory and limb muscles, leading to difficulties in breathing, moving, and performing activities of daily living[1,2]. ICUAW can result from a combination of factors, including immobility, prolonged use of mechanical ventilation, and systemic inflammation[1].

ICUAW is a significant concern in critical care medicine for several reasons including prognostic indicators, impact on functional outcomes, resource utilization, and clinical decision-making[1-3].

The development of ICUAW is associated with increased morbidity and mortality rates among ICU patients. Patients with ICUAW are at higher risk of complications such as pneumonia, sepsis, and prolonged hospital stays. Predicting the development of ICUAW can help clinicians identify high-risk patients early and implement preventive measures to mitigate its impact[1,2]. ICUAW can have long-term consequences on a patient's functional status and quality of life. It can lead to muscle wasting, weakness, and difficulty in performing basic activities, which can impair the patient's ability to return to their pre-ICU level of functioning. Predicting ICUAW can help clinicians develop targeted rehabilitation programs to improve patient outcomes[1,3]. ICUAW can increase the need for prolonged mechanical ventilation, rehabilitation services, and long-term care, leading to increased healthcare costs and resource utilization. Predicting ICUAW can help healthcare providers allocate resources more efficiently and improve the cost-effectiveness of care delivery[1-3]. Predicting ICUAW can inform clinical decision-making regarding the use of sedation, mechanical ventilation, and physical therapy interventions. Early identification of patients at risk of developing ICUAW can guide the implementation of preventive strategies and optimize patient care[2,3].

Overall, predicting the performance of ICUAW is important for improving patient outcomes, optimizing resource utilization, and guiding clinical decision-making in the critical care setting. It allows healthcare providers to identify high-risk patients early and implement targeted interventions to mitigate the impact of ICUAW on patient morbidity and mortality. However, predicting ICUAW is challenging due to its multifactorial nature and the lack of a gold standard diagnostic test[1-3].

However, several methods have been used to assess the risk of ICUAW and predict its development including clinical assessment, electrophysiological testing, biomarkers, muscle ultrasound, and machine learning models[1,4-6]. Clinicians often use a combination of clinical signs and symptoms to assess the risk of ICUAW. These may include muscle weakness, difficulty weaning from mechanical ventilation, and prolonged ICU stay. However, clinical assessment alone may not be sensitive or specific enough to accurately predict ICUAW[1-4]. Electrophysiological tests, such as electromyography and nerve conduction studies, can assess the function of the peripheral nerves and muscles. These tests can detect abnormalities in nerve conduction and muscle activation, which may indicate the presence of ICUAW. However, these tests are invasive, time-consuming, and may not be feasible in critically ill patients[1-3,5-7]. Biomarkers, such as creatine kinase and myosin light chain, have been investigated as potential indicators of muscle injury and ICUAW. Elevated levels of these biomarkers may suggest muscle damage, but their specificity for ICUAW is limited, and they may also be elevated in other conditions[1-3,6,8]. Muscle ultrasound can assess muscle thickness and echogenicity, which may be altered in patients with ICUAW. However, the interpretation of ultrasound findings can be subjective, and the technique may be operator-dependent[1-3,9]. **Table 1** illustrates the strengths and weaknesses of these methods for predicting ICUAW.

Recent studies have explored the use of machine learning models, such as artificial neural networks, to predict ICUAW. These models can analyze large datasets and identify patterns that may be predictive of ICUAW. However, the performance of these models may vary depending on the quality and size of the dataset used for training[1-3,8,9].

## THE MULTILAYER PERCEPTRON NEURAL NETWORK MODEL

The multilayer perceptron (MLP) neural network model is a type of artificial neural network that has been widely used in various fields, including healthcare, for predictive modeling tasks[10]. It is a feedforward neural network with multiple layers of nodes (neurons) that are interconnected by weighted edges. Each node in the input layer represents a feature of

**Table 1 Strengths and weaknesses of existing approaches to predicting intensive care unit-acquired weakness**

Approach	Strengths	Weaknesses
Clinical assessment	Clinicians can use clinical signs and symptoms to assess the risk of ICUAW, which is a non-invasive and readily available method	Clinical signs and symptoms may not be sensitive or specific enough to accurately predict ICUAW
Electrophysiological Testing	Electrophysiological tests, such as electromyography and nerve conduction studies, can provide objective measures of muscle function and help diagnose ICUAW	Electrophysiological tests are invasive, time-consuming, and may not be feasible in critically ill patients
Biomarkers	Biomarkers, such as creatine kinase and myosin light chain, can indicate muscle damage and may be useful for diagnosing ICUAW	Biomarkers are not specific to ICUAW and may be elevated in other conditions
Muscle ultrasound	Muscle ultrasound can provide information about muscle thickness and echogenicity, which can be altered in patients with ICUAW	The interpretation of ultrasound findings can be subjective, and the technique may be operator-dependent

ICUAW: Intensive care unit-acquired weakness.

the input data, and each node in the output layer represents a prediction or classification label. The nodes in the hidden layers perform nonlinear transformations of the input data, allowing the model to capture complex patterns and relationships in the data[11].

The MLP model has several advantages that make it a potential solution to improve prediction accuracy for ICUAW. The MLP model can capture nonlinear relationships between input features and the target variable[11], which is essential for predicting complex medical conditions like ICUAW that may involve multiple interacting factors. The MLP model can automatically learn relevant features from the input data, reducing the need for manual feature engineering and potentially capturing subtle patterns that may be missed by traditional statistical models[12]. The MLP model can be easily scaled to handle large datasets with many features, making it suitable for analyzing electronic health record data and other healthcare datasets[13]. The MLP model can generalize well to new data, making it suitable for predicting ICUAW in different patient populations or healthcare settings[10]. Although MLP models are often considered "black box" models, techniques such as feature importance analysis and model visualization can help interpret the model's predictions[14] and understand the factors that contribute to ICUAW risk. There are several open-source libraries and tools available for building and training MLP models, making them accessible to researchers and clinicians without extensive machine-learning expertise[15].

Overall, the MLP neural network model is a promising approach for predicting ICUAW, and its flexibility, scalability, and ability to capture complex patterns in the data make it a potential solution to improve prediction accuracy for this condition. However, further research is needed to validate the model's performance in larger patient populations and to identify the most effective predictive variables.

## ICU PREDICTION MODELS THAT HAVE USED NEURAL NETWORK AND MACHINE LEARNING MODELS

Several studies have investigated the use of prediction models, including those based on neural networks and machine learning models to assess the risk of ICU and improve patient outcomes.

### Neural network-based models

The study by Benyó *et al*[16] focuses on computational glycemic mechanism (GM) used to manage stress-caused hyperglycemia in ICUs. The Stochastic-TARgeted GM procedure, employed in ICUs across several countries, is a simulation-driven GM procedure that utilizes a personalized, algorithmic insulin sensitivity to explain the individual's current condition. The research presents two methodologies rooted in neural networks for forecasting the individual's insulin sensitivity factor: A deep neural network for classification and a technique based on Mixture Density networks. These methods are trained using treatment data from three distinct patient cohorts. The precision of the neural network forecasts is contrasted with the existing computational model predictions employed in clinical practice, and it is found to be either matching or surpassing the benchmark. The authors propose that these approaches could present a hopeful substitute in computational treatment planning for individual health status prognosis, but they emphasize the need for further research, including in-silico simulations and clinical validation trials, to validate these findings[16].

The study by Pappada *et al*[17] emphasizes the critical importance of achieving glycemic control in patients in ICUs, as it has been associated with reduced mortality, shorter ICU stays, and lower risks of complications such as infection. However, maintaining glycemic control in this setting is challenging due to the diverse range of illnesses and patient conditions. The study collected continuous glucose monitoring (CGM) data and other relevant measures from the electronic medical records of 127 patients for the first 72 h of ICU care. These patients had either type 1 or type 2 diabetes or had a glucose value > 150 mg/dL upon admission to the ICU. The researchers developed a neural network-based model to predict a complete trajectory of glucose values up to 135 min in advance. The model's accuracy was validated using data from 15 patients not included in the training set, simulating real-world healthcare settings. The predictive models showed improved accuracy and performance compared to previous models developed by the research team. The model error, expressed as the mean absolute difference percent, was 10.6% for interstitial glucose values and 15.9% for

serum blood glucose values collected 135 min in the future. A Clarke Error Grid Analysis of model predictions concerning the reference CGM, and blood glucose measurements revealed that over 99% of model predictions could be considered clinically acceptable and would not lead to inaccurate insulin therapy or treatment recommendations. This high level of clinical acceptability suggests that these models could be valuable tools within a clinical decision support system to assist healthcare providers in optimizing glycemic management in critical care patients[17].

The study by Wang and Long[9] recently published in the *World Journal of Clinical Cases*, focuses on identifying significant risk factors for ICUAW and offering recommendations for its prevention and treatment. The study utilized a MLP neural network model to analyze data from the initial 14 d of ICU stay, including age, comorbidities, sedative and vasopressor dosages, duration of mechanical ventilation, length of ICU stays, and rehabilitation therapy. The relationships between these variables and ICUAW were examined. The study found that age, duration of mechanical ventilation, lorazepam and adrenaline dosages, and length of ICU stay were significantly higher in the ICUAW group. Additionally, several comorbidities and conditions were significantly more prevalent in the ICUAW group. The most influential factors contributing to ICUAW were identified as the length of ICU stay and the duration of mechanical ventilation. The neural network model developed in the study predicted ICUAW with high accuracy, sensitivity, and specificity. These findings highlight the importance of minimizing both ICU stay and mechanical ventilation duration as primary preventive strategies for ICUAW.

### Machine learning models

The study by Chang *et al*[18] focuses on predicting the need for ICU admission in patients with myasthenia gravis (MG), an autoimmune neuromuscular disorder characterized by muscle weakness. Although specialized neuro-intensive care can lead to good long-term outcomes, predicting the need for ICU care is critical for optimizing patient management. The study used three machine learning-based decision tree algorithms to predict ICU admission in 228 MG patients admitted between 2015 and 2018. The C5.0 decision tree outperformed the other models and identified several significant risk factors for ICU admission, including the Myasthenia Gravis Foundation of America clinical classification at admission, thymoma history, azathioprine treatment history, disease duration, sex, and onset age. The developed decision tree can serve as a supportive tool for clinicians to identify MG patients who require intensive care, thereby improving the quality of care and potentially reducing morbidity and mortality.

The study by Tran *et al*[8] concentrates on crafting a clinical tool grounded in machine learning to anticipate muscle ailment subcategories utilizing multi-cohort microarray expression information. The information was curated from 42 separate cohorts with expression outlines in publicly available gene sources, encompassing a diverse spectrum of subject ages and muscle tissue samples from non-central regions. The research classified cohorts into five categories of muscle disorders: Limited mobility, inflammatory muscle diseases, ICU-acquired weakness, congenital conditions, and chronic systemic illnesses. The dataset includes evidence on 34,099 genes, and procedures to augment the information was employed to rectify imbalances in subtype representation within muscle disorders. Support direction mechanism algorithms were trained on two-thirds of the 1260 samples using the most significant gene signatures identified through statistical tests. Validation of the model was conducted on the residual testers utilizing the area under the receiver operator curve (AUC). The study found that chronic systemic disease was the best-predicted class with an AUC of 0.872, while ICUAW and immobility were the least discriminated classes with AUCs of 0.777 and 0.789, respectively. Condition-particular gene set enhancement findings revealed that the genetic profile exhibited improvement in biological pathways such as proliferation of neural progenitor cells for ICU-acquired weakness and aerobic metabolism for congenital conditions. The research concludes that the devised molecular categorization instrument featuring the chosen genetic indicators for categorizing muscle disorders fills a notable void in the literature on muscular ailments and introduces a potentially valuable diagnostic aid for discerning muscle disorder variety in clinical practice.

In summary, these investigations underscore the promise of prediction models in evaluating risk and enhancing patient outcomes. Nonetheless, additional research is required to validate these models across larger patient cohorts and to pinpoint the most efficacious predictive variables.

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## DATASET USED TO TRAIN AND TEST THE MLP MODEL

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The dataset used to train and test the MLP model for predicting ICUAW would typically consist of a variety of clinical and demographic variables collected from patients admitted to the ICU. The variables that could be included in the model are presented in [Table 2](#).

The dataset would typically be divided into two subsets: A training set and a test set. The training set would be used to train the MLP model, while the test set would be used to evaluate the model's performance. The dataset may also be divided into a validation set, which is used to tune the model's hyperparameters and prevent overfitting. It is important to note that the dataset should be large enough to adequately represent the patient population and include enough patients who develop ICUAW to allow for meaningful analysis. Additionally, missing data and outliers should be carefully handled to ensure the reliability of the model's predictions.

**Table 2 Variety of clinical and demographic variables collected from patients admitted to the intensive care unit**

Patient profile and assessment	Variable
Demographic information	Age
	Sex
	Race
	Other demographic characteristics of the patient
Clinical characteristics	Comorbidities
	Severity of illness scores ( <i>e.g.</i> , APACHE II, SOFA)
	Reason for ICU admission
Laboratory values	Creatinine
	Liver function tests
	Complete blood count
	Inflammatory markers
Vital signs	Heart rate
	Blood pressure
	Respiratory rate
	Temperature
Medication and treatment	Sedatives
	Analgesics
	Neuromuscular blocking agents
	Other medications
Mechanical ventilation	Duration of mechanical ventilation
	Mode of ventilation
	Ventilator settings
Muscle strength and function	Assessment of muscle strength ( <i>e.g.</i> , Medical Research Council scale, handgrip dynamometer)
Neurological status	Glasgow coma scale score
	Neurological examination findings
	Presence of delirium
Functional status	Pre-ICU functional status ( <i>e.g.</i> , ability to perform activities of daily living)
Outcomes	Development of ICUAW
	Duration of ICU stay
	Duration of mechanical ventilation
	Mortality

ICU: Intensive care unit; ICUAW: Intensive care unit-acquired weakness.

## SPECIFIC FEATURES AND PARAMETERS OF THE MLP MODEL FOR PREDICTING ICUAW

The specific features and parameters of the MLP model for predicting ICUAW can vary depending on the dataset and the specific implementation of the model. However, some common features and parameters must be included, such as the number of layers, activation functions, optimization algorithm, regularization, batch size, learning rate, and dropout rate.

The MLP model typically consists of an input layer, one or more hidden layers, and an output layer. The number of hidden layers and the number of nodes (neurons) in each layer are hyperparameters that need to be determined based on the complexity of the dataset and the desired level of prediction accuracy[11-13,19].

Activation functions are used to introduce nonlinearity into the model, allowing it to capture complex patterns in the data. Common activation functions used in MLP models include the sigmoid function, the hyperbolic tangent function, and the rectified linear unit function[11-14].

The optimization algorithm is used to update the weights of the model during training to minimize the loss function. Common optimization algorithms used in MLP models include stochastic gradient descent (SGD), Adam, and RMSprop [11-14].

Regularization techniques, such as L1 and L2 regularization, are used to prevent overfitting by penalizing large weights in the model. Dropout is another regularization technique that randomly drops a fraction of the nodes in each layer during training to prevent co-adaptation of neurons[11-13].

The batch size is the number of samples used to compute the gradient of the loss function during each iteration of training. A smaller batch size may lead to faster convergence but may result in noisy updates, while a larger batch size may lead to more stable updates but may require more memory[11-14].

The learning rate is a hyperparameter that determines the size of the step taken by the optimization algorithm during each iteration of training. A higher learning rate may lead to faster convergence but may result in overshooting the minimum of the loss function, while a lower learning rate may lead to slower convergence but may result in more stable updates[11-14].

The dropout rate is the fraction of nodes that are randomly dropped during training. A higher dropout rate may lead to more regularization but may result in slower convergence, while a lower dropout rate may lead to faster convergence but may result in overfitting[12-15].

These are just some of the features and parameters that can be used in an MLP model for predicting ICUAW. The specific choices of features and parameters should be based on the characteristics of the dataset and the desired level of prediction accuracy.

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## PROCESS OF TRAINING AND VALIDATING THE MLP MODEL FOR PREDICTING ICUAW

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The process of training and validating the MLP model for predicting ICUAW involves several steps, including data preprocessing, model training, hyperparameter tuning, cross-validation, model evaluation, and interpretation (Figure 1). The step-by-step process is described below.

The first step is to preprocess the dataset by handling missing values, normalizing numerical features, and encoding categorical variables. This ensures that the data is in a suitable format for training the model. Next, the MLP model is trained using the training set. During training, the model's weights are updated iteratively using an optimization algorithm (*e.g.*, SGD) to minimize the loss function. The loss function measures the difference between the model's predictions and the actual outcomes[20]. Hyperparameters are parameters that are not learned during training but are set before training begins. Examples of hyperparameters include the number of hidden layers, the number of nodes in each layer, the learning rate, and the dropout rate. Hyperparameter tuning involves selecting the optimal values for these hyperparameters to improve the model's performance. This can be done using techniques such as grid search, random search, or Bayesian optimization[21]. Cross-validation is a technique used to assess the generalization performance of the model. It involves splitting the dataset into multiple subsets (folds), training the model on some of the folds, and evaluating its performance on the remaining folds. This process is repeated multiple times, with different subsets used for training and evaluation each time. The average performance across all folds is used as an estimate of the model's generalization performance[10]. Once the model has been trained and validated, its performance is evaluated using the test set, which was not used during training or validation. The evaluation metrics used to assess the model's performance may include accuracy, precision, recall, F1 score, and area under the receiver operating characteristic curve[22]. These metrics provide insights into the model's ability to correctly classify patients with and without ICUAW. After evaluating the model, it is important to interpret its predictions and understand the factors that contribute to ICUAW risk. Techniques such as feature importance analysis and model visualization can help identify the most important predictive variables and understand the model's decision-making process[10,21,22]. The process is iterative and may involve multiple rounds of data preprocessing, model training, hyperparameter tuning, cross-validation, model evaluation, and interpretation.

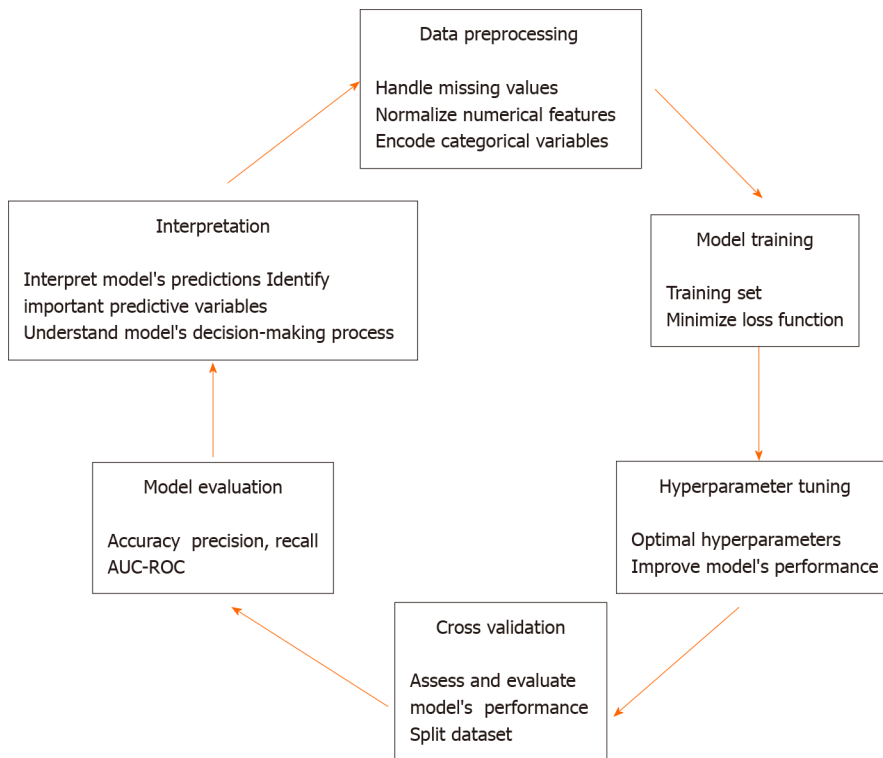
By following these steps, researchers and clinicians can develop and validate an MLP model for predicting ICUAW that is accurate, reliable, and interpretable.

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## CONCLUSION

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This editorial on predicting ICUAW using an MLP neural network model presents a comprehensive approach to addressing the challenges associated with predicting ICUAW. By leveraging the capabilities of the MLP model, researchers and clinicians can develop a predictive model that is accurate, reliable, and interpretable. The editorial highlights the importance of predicting ICUAW for improving patient outcomes, optimizing resource utilization, and guiding clinical decision-making in the critical care setting. The editorial presents the strengths and weaknesses of existing approaches to predicting ICUAW, including clinical assessment, electrophysiological testing, biomarkers, and muscle ultrasound. It emphasizes the limitations of these approaches and how the MLP model addresses these limitations by providing a nonlinear modeling approach, feature learning capabilities, scalability, generalization, and interpretability.



**Figure 1** Training and validating the multilayer perception model for predicting intensive care unit-acquired weakness. AUC-ROC: Area under the receiver operating characteristic curve.

## FOOTNOTES

**Author contributions:** Ardila CM performed the conceptualization, data curation, data analysis, manuscript writing, and revision of the manuscript; González-Arroyave D performed the data analysis, manuscript writing, and revision of the manuscript; Zuluaga-Gómez M performed data analysis, manuscript writing, and revision of the manuscript.

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