PREDICTION OF ARTERIAL BLOOD GAS FROM VENOUS BLOOD GAS: HOW FAR WE’VE COME

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Abstract
Venous blood gas has been extensively studied as a replacement for arterial blood gas, which remains the gold standard despite some drawbacks. Many question the validity of venous blood gas for a routine clinical practice application. Arterial and venous pH are clinically interchangeable with a consistently narrow mean difference (bias: 0.03) and limits of agreement (LOA: -0.1 to 0.1). In contrast, arterial and venous pCO₂ demonstrate a wide LOA (-20 to 20), while arterial and venous pO₂ have a more pronounced difference. Many prediction studies showed a high correlation between arterial and venous pCO₂ (r>0.7) yet a poor correlation between arterial and venous pO₂ (r<0.3), suggesting a non-linear relationship. Leveraging the predictive power of artificial intelligence is paramount to modeling complex non-linear relationships between venous and arterial blood gas parameters, which may improve the estimation of arterial blood gas using venous samples.

Keywords
Blood Gas Analysis, Arterial Blood Gas, Venous Blood Gas

Introduction
Blood Gas Analysis (BGA) is a standard procedure to assess acid-base balance disorder and oxygenation status due to respiratory or metabolic problems. BGA directly measures pH, partial pressure of carbon dioxide (pCO₂), partial pressure of oxygen (pO₂), and derived values of bicarbonate (HCO₃⁻), base excess, and anion gap.¹ BGA is essential for patient management, particularly in emergencies.²
The arterial sample remains the gold standard as its composition is consistent despite any changes in systemic circulation and is unaffected by tissue metabolism. The radial artery is a common site for taking BGA samples, considering its superficial location and adequate collateral circulation. However, due to its relatively small size, arterial sampling is often challenging, with an increased risk of needle stick injury. Arterial sampling is also frequently reported as painful and exacerbated by repeated sampling attempts. The most common complications of arterial sampling are hematoma, infection, and hemorrhage. Other rare but rather severe complications are thrombosis, embolism, dissection, aneurysm, and compartment syndrome.

Based on the limitations of arterial sampling, many researchers proposed venous blood gas as an alternative to arterial blood gas samples. Venous samples are more accessible, time-saving, and can be sampled for other laboratory tests. Moreover, they are less invasive, with a negligible risk of vascular complications, and more comfortable for patients.

**Comparison between Arterial and Venous Blood Gas**

Researchers have conducted extensive studies on using venous samples as an alternative to arterial samples. Before regular application in various clinical settings, venous blood gas needs confirmation of good reliability and acceptable agreement with arterial blood gas. Different measurement techniques are comparable using the Bland-Altman method. The difference between the two measurement techniques is called bias in the Bland-Altman method. The standard deviation of the mean differences is called the Limits of Agreement (LOA). LOA determines how far apart the calculations of the two methods are for most individuals. Two methods are considered interchangeable if the bias is slight and the range of the LOA is not clinically significant.

Some differences exist between arterial and venous blood gas, where arterial samples have a higher pH and pO₂ but lower pCO₂. A survey was conducted on 26 clinicians to determine the tolerated range of LOA on blood gas parameters. The clinically acceptable ranges of LOA for pH, pCO₂, and HCO₃⁻ were 0.05, 6.6, and 3.5, respectively.

Based on a meta-analysis of 18 studies involving 1,768 subjects, there is a slight difference between arterial and venous pH. The arterial pH was 0.033 units higher than the venous pH (LOA ranging from 0.029 to 0.038). In contrast, arterial and venous pCO₂ had a wide bias of -4.15 mmHg (LOA ranging from -5.54 to -2.77). Likewise, arterial and venous pO₂ had a broader bias of 36.9 mmHg (LOA ranging from 27.2 mmHg to 46.6 mmHg). Another meta-analysis centered on the emergency department yielded a similar bias of arteriovenous pH and pCO₂ but showed an even broader LOA for pCO₂ of -25.8 to 20.4.
Specific conditions such as COPD exacerbations still generated consistent results as in the previous meta-analysis. Bias of arteriovenous pH, pCO₂, and pO₂ were 0.028, -5.92, and 18.65, respectively, with LOA of pH and pCO₂ ranging from -0.10 to 0.08 and from -17 to 26.¹⁸

Venous pH can be utilized as an alternative to arterial pH since it consistently shows a narrow bias of 0.03 and LOA ranging from -0.1 to 0.1. Conversely, due to significant differences and a wide range of LOA (up to ±20 for pCO₂) exceeding the predetermined clinical agreement, venous pCO₂ and pO₂ are not interchangeable.¹⁴,¹⁹

Some conditions affecting blood flow, such as heart failure, shock, and respiratory failure, may result in more significant differences between arterial and venous samples. However, there is limited research on the influence of systemic circulation on venous blood gas.

**Correlation between Arterial and Venous Blood Gas**

To overcome the poorly comparable arteriovenous pCO₂ and pO₂, researchers attempted to predict arterial from venous blood gas samples using a regression model.²⁰ Blood gas analysis performed in the emergency unit showed strong correlations between arterial and venous pH (r=0.913), pCO₂ (r=0.921), and HCO₃⁻ (r=0.953).¹⁶ Another study in the emergency unit demonstrated a similar correlation between arterial and venous pH (r=0.95), pCO₂ (r=0.83), and HCO₃⁻ (r=0.98).³

Previous studies also examined the correlation between arterial and venous samples under specific conditions. A study on patients in the ICU showed a correlation of pH, pCO₂, and HCO₃⁻ of 0.783, 0.705, and 0.846, respectively.²¹ Another study on patients with chronic uremia and diabetic ketoacidosis obtained a correlation between arterial and venous pH, pCO₂ of 0.979 and 0.989. Meanwhile, arterial and venous pO₂ demonstrated a weak correlation (r<0.3).²²

Various other studies in different medical conditions also suggested a strong correlation between arterial and venous pH and pCO₂, including patients with COPD,²³,²⁴ patients with mechanical ventilation assistance,¹⁰ and other studies in the intensive care unit.²⁰,²⁵

Along with,²² several studies consistently showed a weak association between arterial and venous pO₂, with reported correlations of 0.287, 0.21, and 0.202.³,¹⁰,²⁰ In conclusion, venous blood gas is applicable for predicting arterial blood gas values of pCO₂ and HCO₃⁻. In contrast, venous samples cannot accurately predict the pO₂ value of arterial blood gas samples.²⁶ Therefore, a more advanced method is necessary to precisely determine arterial pO₂ or other arterial blood gas parameters based on venous samples.

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¹ Pearson’s r as the correlation coefficient
Use of Artificial Intelligence to Predict Arterial from Venous Blood Gas

Artificial intelligence (AI) has developed rapidly over the past decade. It is a computational process mimicking the human brain's capabilities. AI has made an impact in almost every field, including medicine.\textsuperscript{27}

Artificial Neural Network (ANN) is the most frequently used AI method for prediction.\textsuperscript{28} ANN is a mathematical representation of the human neural architecture. Information processing occurs in elements called neurons. Neurons are organized in layers. The structure of ANN is formed by an input layer, one or more hidden layers and the output layer. Informations received by neurons in the input layer are then transferred to the output layer through the hidden layer. The hidden layer helps network to recognize still more patterns. By adding more neurons in the hidden layer or more hidden layers, ANN can learn to solve complex nonlinear problems, which brings on the potential to predict arterial blood gas parameters based on venous blood gas more accurately.\textsuperscript{29}

ANN models possess such characteristics as adaptive learning (ability to modify its internal structure), noise-insensitive (fault-tolerance), fast processing (due to parallel computation), and generalization ability (application of the model to untrained data). ANN does not require many assumptions, as in conventional statistics, and a selection of training algorithms is available to fit specific cases.\textsuperscript{28,30}

Only one research reported predicting arterial blood gas from venous blood gas samples using ANN. This study implemented a backpropagation learning algorithm on 132 samples of acute exacerbation COPD patients (80 as training data, 26 as testing data, and the remaining samples for network validation). The study compared the performance of ANN with a linear regression model. The results of the coefficient of determination ($R^2$) of ANN for pH, pCO$_2$, HCO$_3^-$, pO$_2$, and saO$_2$ were 0.945, 0.912, 0.828, 0.676, and 0.712, while the linear regression model had the results of 0.668, 0.487, 0.627, 0.506 and 0.530, respectively. In addition, this study also conducted a sensitivity analysis to detect arterial hypercarbia (arterial pCO$_2$ > 50 mmHg). The results of the sensitivity, specificity, positive predictive value, and negative predictive value of ANN were 88.24, 88.89, 93.75, and 80, whereas the results of linear regression were 94.12, 33.33, 72.72, and 75, respectively.\textsuperscript{9}

In conclusion, this study showed that ANN performed better than linear regression for predicting blood gas parameters. Thus, it carried the potential to solve the weak correlation while predicting the pO$_2$ value, although one thing to consider from this study is that the data distribution did not align with the meta-analysis, as mentioned earlier; the bias of arteriovenous pO$_2$ was much smaller. A comparison of sensitivity analysis showed that ANN had better specificity, positive predictive value and negative predictive value, whereas linear regression slightly outperformed ANN in sensitivity.
Conclusion

Artificial Intelligence (AI), specifically artificial neural networks, addresses the nonlinearity of arterial blood gas prediction from venous blood gas parameters. Future research shall employ large samples, proper data distribution, and diverse sample selection. More evidence is necessary before venous blood gas applies to BGA in clinical settings.

Conflict of Interests
The authors have no conflict of interest to declare.

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