Original Article

Systematic review and meta-analysis: value of venous blood gas in the diagnosis of acute exacerbation of chronic obstructive pulmonary disease in Emergency Department

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Background: at present, arterial blood gas (ABG) analysis is widely used in the diagnosis and treatment evaluation of acute exacerbation of chronic obstructive pulmonary disease (COPD) in emergency department, but it has the risk of thrombosis and bleeding. In recent years, venous blood gas (VBG) analysis has become more and more popular, but its clinical diagnostic value in emergency patients with acute exacerbation of COPD remains unclear.

Methods: relevant clinical studies on the diagnosis of acute exacerbation of COPD by blood gas analysis were searched in Medline, Excerpta Medica Database (EMBASE), Elton B. Stephens. Company (EBSCO), OVID, China Biomedical Database, and Wanfang Database from the establishment of the database to January 2010 to September 2021, Meta-analysis was performed on the data with RevMan5.3. The differences of blood gas analysis indicators potential of hydrogen (pH), partial pressure of carbon dioxide ($PaCO_2$), and hydro-carbonate (HCO_3) were compared between the arterial blood gas group and the venous blood gas group. Heterogeneity of results was assessed with Chi^2 test and I^2 in RevMan5.3.

Results: a total of 7 articles with 1,257 subjects were included in this study. Newcastle-Ottawa scale (NOS) scores were higher than six points. In relation to the ABG analysis and VBG analysis, there was no significant difference in the potential of hydrogen (pH) [mean difference (MD) =–0.00, 95% confidence interval (CI) =0.05–0.04, Z=0.19, P=0.85]; however, there were significant differences in the partial pressure of carbon dioxide ($PaCO_2$) (MD =5.32, 95% CI =3.32–7.33, Z=5.20, P<0.00001) and hydro-carbonate (HCO_3) (MD =1.05, 95% CI =0.27–1.83, Z=2.63, P=0.009).

Conclusions: there were differences between ABG and VBG in the diagnosis of patients with acute exacerbation of COPD in the emergency department. Due to the small number of included literatures, further verification is needed.

Keywords: Chronic obstructive pulmonary disease in acute exacerbation (AECOPD); blood gas analysis; potential of hydrogen (pH); partial pressure of carbon dioxide ($PaCO_2$); hydro-carbonate (HCO_3)

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Introduction

Chronic obstructive pulmonary disease (COPD) is a pulmonary disease for which airflow limitation is the main manifestation. The airflow limitation is completely irreversible and shows progressive development. The causes of its pathogenesis are complex and diverse, and include changes in the internal and external structures and functions of the lungs, and inflammation. Due to the large number of patients with COPD and its high mortality rate, it has now become a public-health concern, and its morbidity and mortality rates continue to increase year by year (1). COPD is a common chronic respiratory disease in our country. Currently, it occupies the first place in the burden of disease. COPD not only seriously affects the life and health of patients, but also places a huge economic burden on patients. The global annual medical expenditure for COPD is about 24 billion U.S. dollars, and 70% of the expenditure is related to acute exacerbation that requires hospitalization.

The acute exacerbation of COPD (AECOPD) is a developmental process of COPD. For a long time, it has been neglected because it is believed to have little effect on the course of the disease. Studies have estimated that on average COPD exacerbations occur 2.5–3 times per year per patient (2,3). Further, the frequency of the exacerbations increases with the severity of the disease, and about half of the exacerbations do not attract the attention of patients. Repeated acute exacerbation is an important clinical feature of COPD, and is not only related to significant physiological decline, but also to increased airway inflammation caused by viruses, bacteria, and air pollution (4). Repeated exacerbation not only affects the health of individuals, but also leads to increased medical expenses and mortality. The effect of the acute exacerbation of chronic obstructive swelling in the prognosis of the disease is still relatively serious; thus, the acute exacerbation of chronic obstructive swelling diagnosis and treatment require attention (5,6).

A blood gas analysis is an important examination that is used to assess the severity of AECOPD and guide the treatment of mechanical assisted ventilation. It plays a vital role in the rescue and monitoring of critical illnesses. COPD blood gas abnormalities first manifest as mild or moderate hypoxemia, and as the disease progresses, the hypoxemia gradually worsens, and hypercapnia appears (7). At present, there are two main types of clinical blood gas examinations; that is, arterial blood gas (ABG) analysis and venous blood gas (VBG) analysis (8).

Arterial blood gas analysis, as the gold standard for evaluating oxygenation and acid-base analysis, can indirectly assess lung function levels through arterial blood gas analysis (9), ABG analysis occupies an important position in the diagnosis and treatment of the acute exacerbation of chronic obstructive swelling disease, as it accurately provides important information, including information about the cause and severity of the disease. In recent years, as the technology continues to mature, the information it provides has become more abundant and diverse (10). However, ABG analysis may take a long time in emergency application, and may lead to the risk of arterial injury and thrombosis (11). VBG analysis method based on real-time analyzer in emergency department can provide patients' coagulation function, pH, and electrolyte status quickly, which can greatly reduce the risk borne by patients in the process of arterial blood collection, reduce iatrogenic injury, and reduce medical costs. Timely determination of the severity of the disease and implementation of intervention measures can provide effective help for the treatment of patients (12). It plays an important role in the diagnosis and treatment of emergency diseases. However, it is still controversial whether VBG analysis can completely replace ABG analysis in AECOPD diagnosis. Some researchers believed that venous and arterial blood flow disease status may lead to differences between VBG and ABG measurement variables, and that factors such as heart failure and obesity may affect the results of VBG analysis (13). Therefore, the clinical application value of VBG in the diagnosis of AECOPD needs further discussion and research. To systematically evaluate the clinical application value of VBG in the diagnosis of AECOPD, meta-analysis was implemented to evaluate the difference between ABG and VBG in the diagnosis of AECOPD, providing a reference basis for the diagnosis and treatment of patients with AECOPD in clinical emergency. We present the following article in accordance with the MOOSE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-22-336/rc).

Methods

Articles retrieval strategies

Databases, including Medline, Excerpta Medica Database (EMBASE), Elton B. Stephens. Company (EBSCO), OVID, China Biomedical Database, and Wanfang, were searched using combinations of the related keywords and medical heading terms related to the blood gas analysis of patients with AECOPD. The search period ran from the establishment of the databases to September 2021. The following keywords were used: chronic obstructive pulmonary disease, COPD, blood gas analysis, emergency, acute exacerbation, case-control study, cohort study, and risk factors. The full texts of the target articles were obtained in accordance with the pre-established inclusion and exclusion criteria. The references in the searched articles were also manually searched to avoid any important documents being missed.

Inclusion and exclusion criteria of the included articles

To be eligible for inclusion in the meta-analysis, the articles had to meet the following inclusion criteria: (I) Concern a case-control or cohort study; (II) comprise patients with AECOPD; (III) examine the measurement outcomes of potential of hydrogen (pH), partial pressure of carbon dioxide ($PaCO_2$), and hydro-carbonate (HCO_3); (IV) use the inspection methods of ABG and VBG analyses; and (V) have data available for analysis, such as relative risk or odds ratio (OR) and 95% confidence interval (CI) data.

Articles were excluded from the meta-analysis if they met any of the following exclusion criteria: (I) had no effect size available for analysis (i.e., lacked cases or control numbers); (II) did not provide original data (i.e., was a comment, series report, letter, case report, or concerned zoology studies or in-vivo studies); and/or (III) only reported deaths.

Articles screening

The articles were independently screened by two researchers, who also extracted and cross-checked the data. If differences in opinions arose, experts were consulted to decide the data selection issue.

Data extraction

The two researchers independently read the articles and determined whether each article was a case-control or cohort study, and whether the data was complete. The articles were excluded or excluded in the meta-analysis based on the above-mentioned criteria. The quality of each article was evaluated, and duplicate reports, articles of poor quality, and those in which the researchers had little confidence were excluded. The data were extracted according to the established tables, and a database was established to check the data. If a research report was incomplete, the author was contacted and the full text was requested, and if the author confirmed that the article was unavailable, it was excluded from this study. If a disagreement arose between the two researchers, the issue was discussed with a third party.

After the full text was obtained, the data were extracted. If there were repeated reports, the most recent research article was selected. The data extracted for this study included basic information about the articles (i.e., the article title, first author, publication year, author information, and source), the basic characteristics of subjects (i.e., gender, age), the research methods, the research plan design, the intervention measures for the experimental group and the control group, the outcome evaluation indicators, and the outcome data.

Quality evaluation

The Newcastle-Ottawa Scale (NOS) was used to evaluate the literature quality. The NOS mainly includes three parts and eight aspects. NOS includes 4 points for study population selection, 2 points for comparability between groups, 3 points for proper measurement of exposure factors, or 3 points for proper measurement of results. There is a full score of 9, and 6 points or more suggests high quality literature.

Statistical analysis

Meta-analysis of the included literatures was performed using RevMan5.3, and the quality of the literatures was evaluated using NOS. The calculation method used the odds ratio (OR) as the effect size, and the 95% confidential interval (CI) was adopted to express the results. For the analysis of heterogeneity, the chi-square test was used to conduct a preliminary test of the heterogeneity of the literature, and the significance level of the test was set as α=0.05, and P<0.05. Quantitative assessment of heterogeneity results was then performed using I^2 in RevMan5.3. When I^2<25%, the literature had low heterogeneity; when 25%<I^2<50%, the literature had moderate heterogeneity; when I^2>50%, the literature had substantial heterogeneity. Hence, when I^2<50%, a fixed-effect model was used for meta-analysis; when I^2>50%, a random-effects model was used for meta-analysis. A funnel chart was used to analyze the publication bias of each risk factor. RevMan5.3 was used to output the forest plot, and the Z value and P value in the results were extracted to judge the results of meta-analysis. Each effect size was

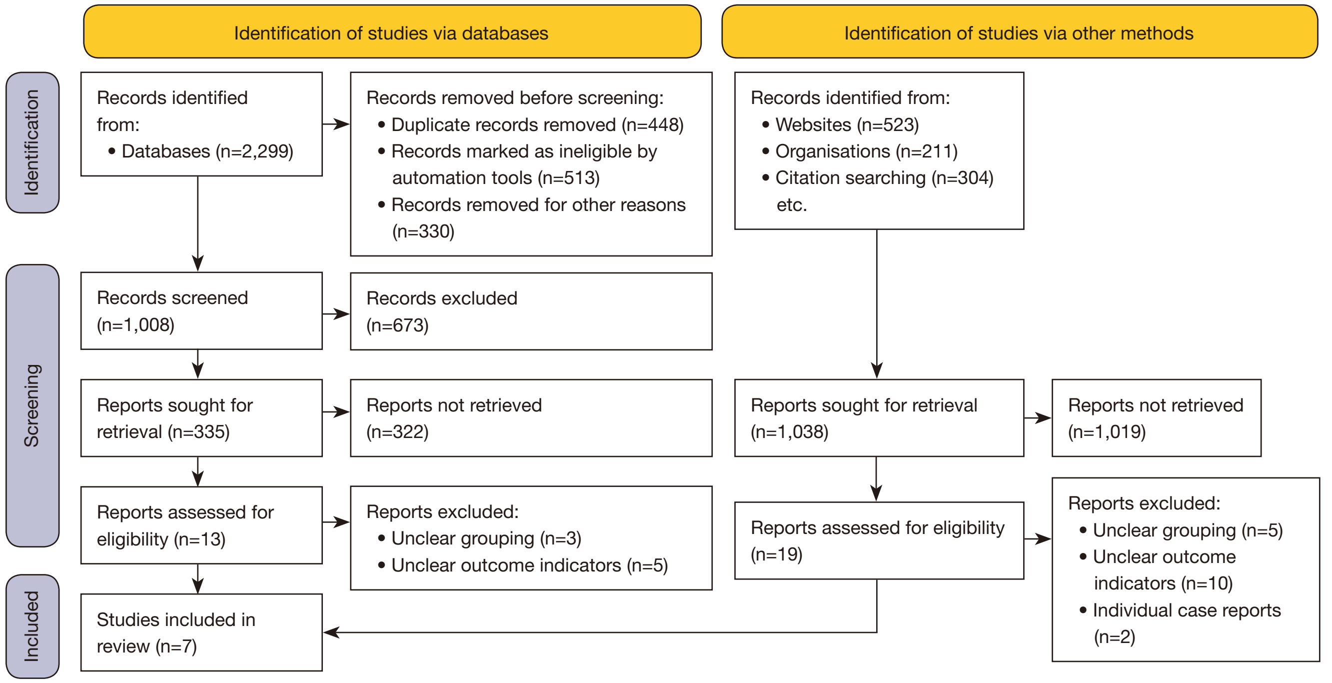

Figure 1 Document retrieval process.

Table 1 Basic information of included articles

First author	Experimental	Controls	Year of publication	Country	NOS score
Rang LC (14)	218	62	2002	China	7
Kelly AM (15)	107	107	2005	Australia	8
Ak A (16)	132	132	2006	China	8
Ibrahim I (17)	122	122	2011	America	7
O'Connor TM (18)	30	30	2011	UK	8
McCanny P (19)	59	30	2012	America	7
Kelly AM (20)	53	53	2013	Australia	8

NOS, Newcastle-Ottawa scale.

expressed by 95% confidence interval (CI), and P<0.05 indicated that the difference was statistically significant.

Results

Basic information and quality assessment of literature

A total of 3,337 related articles were retrieved in this study, of which 2,299 were retrieved from the databases and 1,038 were retrieved manually. Through a series of screening, a total of 3,330 irrelevant and unsatisfactory articles were finally excluded. Ultimately, 7 articles (14-20) that met the inclusion criteria were included in the meta-analysis. The NOS was used to evaluate the quality of the literature, 3 articles were scored 7 points, and 4 articles were scored 8 points, suggesting that the quality of the included literature was high. The details and NOS scores are shown in *Figure 1* and *Table 1*.

pH detection

Of the 7 articles, 5 (14,16,18-20) compared and studied the

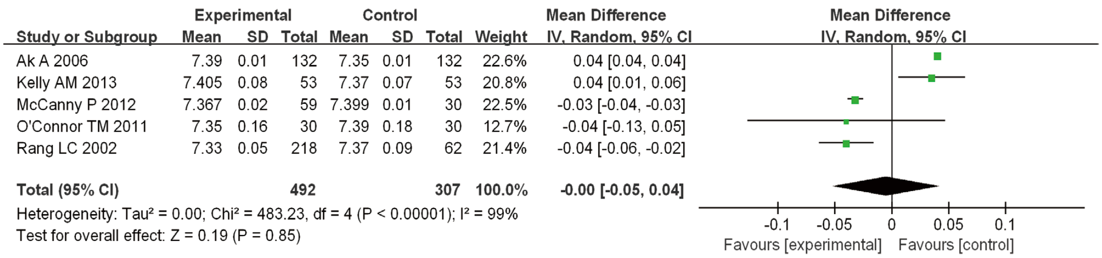

Figure 2 Forest diagram of the pH detection results. pH, potential of hydrogen; SD, standard deviation; CI, confidence interval.

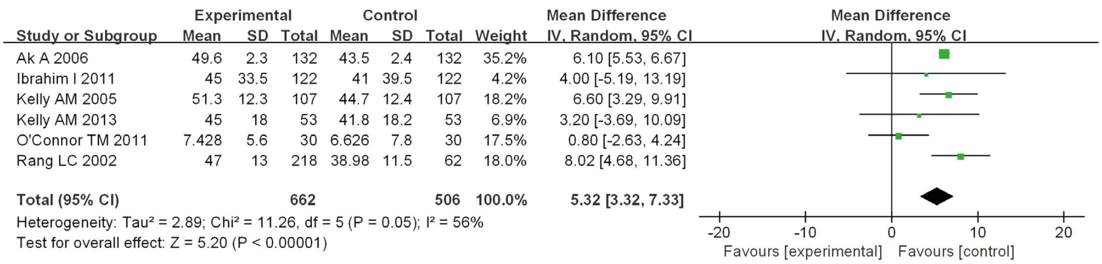

Figure 3 Forest diagram of the $PaCO_2$ detection results. $PaCO_2$, partial pressure of carbon dioxide; SD, standard deviation; CI, confidence interval.

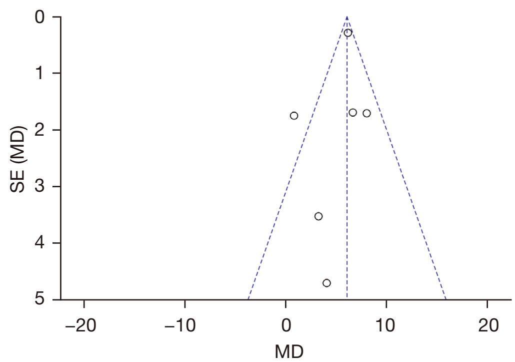

Figure 4 Funnel chart of the $PaCO_2$ detection results. $PaCO_2$, partial pressure of carbon dioxide; SE, standard error; MD, mean difference.

pH values of the ABG and VBG analyses of the AECOPD patients. A meta-analysis was performed on the content of the blood gas analyses and pH of these 5 articles, and it was found that I^2=99% and P<0.00001. As the I^2 was >50%, there was heterogeneity among the articles, and thus the random-effects model (REM) was selected. The meta-analysis results were as follows: mean difference (MD) =–0.00, 95% CI =–0.05 to 0.04, Z=0.19, and P=0.85. Thus, there was no significant difference between the upper ABG and VBG analyses in the pH test results of the AECOPD patients. A forest diagram of the analysis of the pH detection results is shown in *Figure 2*.

$PaCO_2$ detection

Of the 7 articles, 6 (14-18,20) compared and studied the $PaCO_2$ values of the ABG and VBG analyses of the AECOPD patients. A meta-analysis was performed on the content of the blood gas analyses and the $PaCO_2$ values of these 6 articles, and it was found that I^2=56% and P=0.05. As the I^2>50%, there was heterogeneity among the articles, and thus the REM was selected. The meta-analysis results were as follows: MD =5.32, 95% CI =3.32–7.33, Z=5.20, and P<0.00001. Thus, there was no significant difference between the upper ABG and VBG analyses in the $PaCO_2$ values of the AECOPD patients. A forest diagram of the analysis of the $PaCO_2$ detection results is shown in *Figure 3*. *Figure 4* shows a funnel chart of the analysis of pCO_2 detection results. As *Figure 4* shows, the funnel chart was basically symmetrical, and most of the data corresponded to points within the 95% CI, which indicated that publication bias was effective.

HCO_3 detection

Of the 7 articles, 3 articles (14,16,20) compared and studied

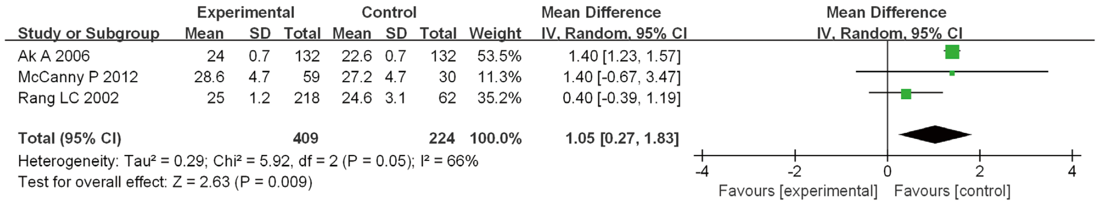

Figure 5 Forest diagram of the HCO_3 detection results. HCO_3, hydro-carbonate; CI, confidence interval.

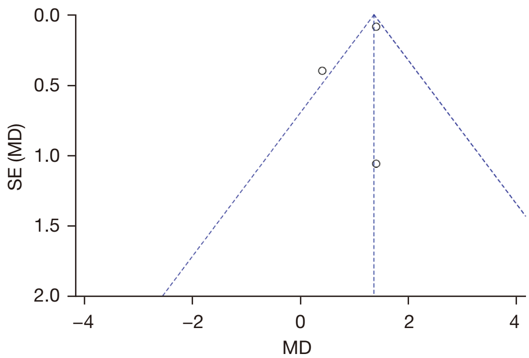

Figure 6 Funnel chart of the HCO_3 detection results. HCO_3, hydro-carbonate; SE, standard error; MD, mean difference.

the HCO_3 values of the ABG and VBG analyses of the AECOPD patients. A meta-analysis was performed on the content of blood gas analysis and HCO_3 values of these 3 articles, and it was found that I^2=66% and P=0.05. As the I^2 was >50%, there was heterogeneity among the articles, and thus the REM was selected. The meta-analysis results were as follows: MD =1.05, 95% CI =0.27–1.83, Z=2.63, and P=0.009. Thus, there was an obvious difference between the ABG and VBG analyses of the HCO_3 values of the AECOPD patients. A forest diagram of the analysis of the HCO_3 detection results is shown in *Figure 5*. *Figure 6* shows a funnel chart of the analysis of the pCO_2 detection results. As *Figure 6* shows, the funnel chart was basically symmetrical, and most of the data corresponded to points within the 95% CI, which indicated that the publication bias was effective.

Discussion

COPD is a disease characterized by airflow limitations, is incompletely reversible and progressive, and is related to the abnormal inflammatory response of the lungs to harmful gases or harmful particles. Under the action of a variety of pathogenic factors, alveolar macrophages produce a variety of neutrophil chemotactic factors, including interleukin-8 and leukotriene B4, so that neutrophils release elastase and other proteolytic enzymes, causing damage to the entire airway and lung parenchyma (21). When patients are in acute exacerbation, due to increased oxygen consumption and respiratory load, and exceed the self-compensation limit, severe hypoxemia and hypercapnia, respiratory failure, or the exacerbation of original respiratory failure may result (22). Thus, AECOPD poses a great threat to the life and health of patients. Research has shown that as the environment and climate continue to deteriorate, the frequency of the occurrence of AECOPD continues to increase year by year (23). For a long time, people have paid little attention to AECOPD; however, the disease poses a huge threat to people's health and quality of life. Thus, it is necessary to conduct in-depth examination on the diagnosis of and treatment methods for AECOPD.

Clinically, blood gas analysis is an important method and means by which emergency departments can evaluate the condition and progress of AECOPD patients. Generally, there are two types of blood gas analyses; that is, ABG and VBG (24-26). The ABG analysis is the gold standard test for clinical evaluations of the ventilation status of AECOPD patients. It not only helps doctors determine a patient's ventilation and acid-base status, but also helps doctors determine whether further medication and non-invasive ventilation are needed (27-29). There are many advantages for ABG, and ABG plays a pivotal role in the diagnosis and treatment of AECOPD patients. However, the ABG analysis also has some limitations. For example, the sampling time for an ABG analysis is accompanied by the risk of bleeding, hematoma, infection, nerve damage, finger ischemia, and other vascular diseases (30,31). Further, blood sampling requirements also increase the risk of staff injury. Conversely, the VBG analysis can be conducted when a patient is intubated, and the pain and risk to patients are relatively low (32). Thus, the VBG analysis is becoming more and more popular in clinical practice, and more and more studies are being conducted on ABG and VBG analyses.

To date, a study has investigated the possibility of VBG sampling instead of ABG sampling in emergency situations (33). One study found a good correlation between the venous and arterial values of pH, but only a small correlation with $PaCO_2$ (34). A previous study has shown that venous $PaCO_2$ can predict arterial hypercapnia (35). There is more and more evidence to support the value of VBG sampling in the evaluation of patients with acute respiratory diseases in the emergency department, but there are also reports of research results that are consistent with the above viewpoints. For example, a study has shown that there is a significant difference between arterial and venous pH in pediatric patients (36). The relevant result indicators of a blood gas analysis can be affected by many factors, which may be the reason for the different results of these studies. Thus, further research needs to be conducted on the clinical application value of the VBG analysis and whether it can completely replace the ABG analysis.

In this study, articles related to the blood gas analysis of AECOPD patients were retrieved to analyze the consistency of the ABG and VBG examination results in relation to three indicators (i.e., $PaCO_2$, pH, and HCO_3). We found that the ABG and VBG analyses had significant differences in terms of $PaCO_2$ and pH, but were more consistent in terms of HCO_3. Thus, the VBG analysis has certain clinical application value in the diagnosis of AECOPD patients, but the question of whether it can replace the ABG analysis requires further discussion.

Conclusions

In this study, articles related to the blood gas analysis of AECOPD patients were retrieved to analyze the consistency of the ABG and VBG examination results in relation to three indicators (i.e., $PaCO_2$, pH, and HCO_3). We found that the ABG analysis and the VBG analysis had significant differences in terms of $PaCO_2$ and pH, but were more consistent in terms of HCO_3. Thus, the VBG analysis has certain clinical application value in the diagnosis of AECOPD patients, but the question of whether it can replace the ABG analysis requires further discussion. This study provided a reference and basis for the clinical diagnosis and treatment of AECOPD patients. However, as the articles included in this study were not sufficiently comprehensive and rich, there may be some deviations in the research results of this study. In the future, we intend to further expand the scope of our search to undertake more in-depth and comprehensive research.

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Footnote

Reporting Checklist: The authors have completed the MOOSE reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-22-336/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-22-336/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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