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Efficacy and Safety of Airway Stent Placement in the Treatment of Airway Esophageal Fistula

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Keywords
Esophageal cancer · Airway esophageal fistula · Airway stent · Conservative care · Efficacy

Abstract

Introduction: This study aimed to evaluate both the clinical efficacy and safety of airway stent placement in the treatment of patients with esophageal cancer-associated airway esophageal fistula (AEF). The focus is on evaluating improvements in patient survival and quality of life. ***Methods:*** Overall, this study enrolled 111 patients diagnosed with esophageal cancer-associated AEF. Among them, 50 (45.0%) and 61 (55.0%) patients received airway stent placement and conservative treatment, respectively. Follow-up assessments were conducted to determine the clinical efficacy and safety of the interventions, with survival and quality of life as the primary endpoints. ***Results:*** By the end of the follow-up, 98 of 111 patients (88.3%) had died, leaving 13 survivors (11.7%). Patients with esophageal cancer-associated AEF had an overall mean survival time of 147.4 (95% CI, 123.9–170.9) days. Patients in the stent placement group had a mean survival of 192.5 (95% CI, 151.2–233.7) days, which was significantly longer than the 110.0 (95% CI, 88.1–131.8) days in the conservative treatment group ($p < 0.001$). Sex ($p = 0.017$), tumor stage ($p = 0.030$), surgery ($p = 0.005$), pulmonary infection ($p < 0.001$), fistula size ($p < 0.001$), and pre-Karnofsky Performance Status (KPS) ($p < 0.001$) were the independent risk factors affecting survival. Furthermore, patients in the stent placement group demonstrated improved KPS scores post-treatment, increasing from 48.2 to 57.9 ($p = 0.017$). ***Conclusion:*** Airway stent placement is beneficial in alleviating the symptoms, quality of life, and survival of patients with esophageal cancer-associated AEF.

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Introduction

Esophageal cancer, a highly aggressive malignancy, ranks among the leading causes of cancer-related deaths worldwide [1]. Its prevalence is particularly increasing in developing countries, accounting for a significant portion of cancer diagnoses [2]. With a global 5-year survival rate of only 20%–30%, patients diagnosed with esophageal cancer frequently develop life-threatening complications that markedly affect their quality of life [3]. The development of an airway esophageal fistula (AEF), which is characterized by an abnormal connection between the esophagus and the airway, is one of the most critical complications [4]. This condition typically arises either as the cancer progresses or secondary to therapeutic interventions, including radiation or chemotherapy.

AEF can cause severe respiratory complications, including aspiration pneumonia and respiratory failure, which complicate management and treatment efforts [5, 6]. Esophageal cancer-related AEF has historically presented significant treatment challenges owing to its complex and fragile nature [7]. The commonly used treatment method is conservative treatment, mainly encompassing supportive care, antibiotics, and nutritional support [8]. Although conservative treatment can help reduce the incidence of complications and improve patients' quality of life, it frequently does not significantly improve the overall survival prognosis of patients [9]. Moreover, surgery is an option; however, patients with malignant AEF are frequently malnourished and are usually undergoing chemotherapy and/or radiation, making them poor surgical candidates [10].

Airway stent placement has recently emerged as a promising treatment modality, offering a minimally invasive solution for sealing the fistula and preventing esophageal contents from entering the airway, thereby improving patient outcomes [11–14]. This study aimed to evaluate the clinical efficacy and safety of airway stent placement compared with conservative treatment, particularly in prolonging survival and enhancing the quality of life for patients who developed AEF secondary to esophageal cancer.

Materials and Methods

Patient Population

This retrospective study analyzed the medical records of patients with esophageal cancer who were diagnosed with AEF over a 7-year period. The cohort comprised patients treated at Henan Provincial People's Hospital between January 1, 2017, and March 1, 2024. A total of 111 patients, each fulfilling the inclusion and exclusion criteria, were included in this study. The following were the inclusion criteria: (1) aged >18 years, (2) patients who met the World Health Organization diagnostic criteria for esophageal cancer, and (3) esophageal cancer combined with AEF. The following were the exclusion criteria: (1) patients with early stage cancer for which surgery was an option; (2) other types of malignant tumors combined with AEF; (3) other types of esophageal fistula, including esophageal-mediastinal fistula; and (4) patients with incomplete medical records. These criteria ensured that the study population was homogeneous and relevant to the study's objectives.

The patients were categorized into two groups on the basis of their treatment approach. Fifty patients (45.0%) underwent airway stent placement, including silicone and tract-covered metal stents. The remaining 61 patients (55.0%) received conservative treatments, encompassing supportive care, antibiotics, and nutritional support (Fig. 1). The choice of treatment was determined on the basis of the patient's clinical status and the physician's expertise. The stent placement group underwent a minimally invasive procedure in which an airway stent was inserted to prevent esophageal content leakage into the respiratory system. Conversely, the conservative care group received noninvasive treatments aimed at symptom management and complication reduction.

Data Collection

To facilitate a detailed analysis of treatment outcomes, comprehensive data were collected for each patient. Demographic variables encompassed age, sex, and smoking status. To assess the progression and complexity of the disease, clinical data, including tumor stage (T0–T3 or T4), tumor location (neck/upper, middle, or lower esophagus), location of the fistula in the airway (trachea, left main bronchus, right main bronchus, or multiple sites), and the size of the fistula, were documented. Furthermore, we added the pre-Karnofsky Performance Status (KPS) to represent the patient's physical condition. These variables were essential for evaluating the baseline characteristics of the patients and comparing treatment outcomes across different subgroups.

Along with demographic and clinical data, information regarding each patient's medical history, including previous surgery and prior treatments (chemotherapy, radiotherapy, or immunotherapy), was gathered to provide context for their overall health status. Complications, including pulmonary infections, stent-related issues, and other adverse events, were meticulously

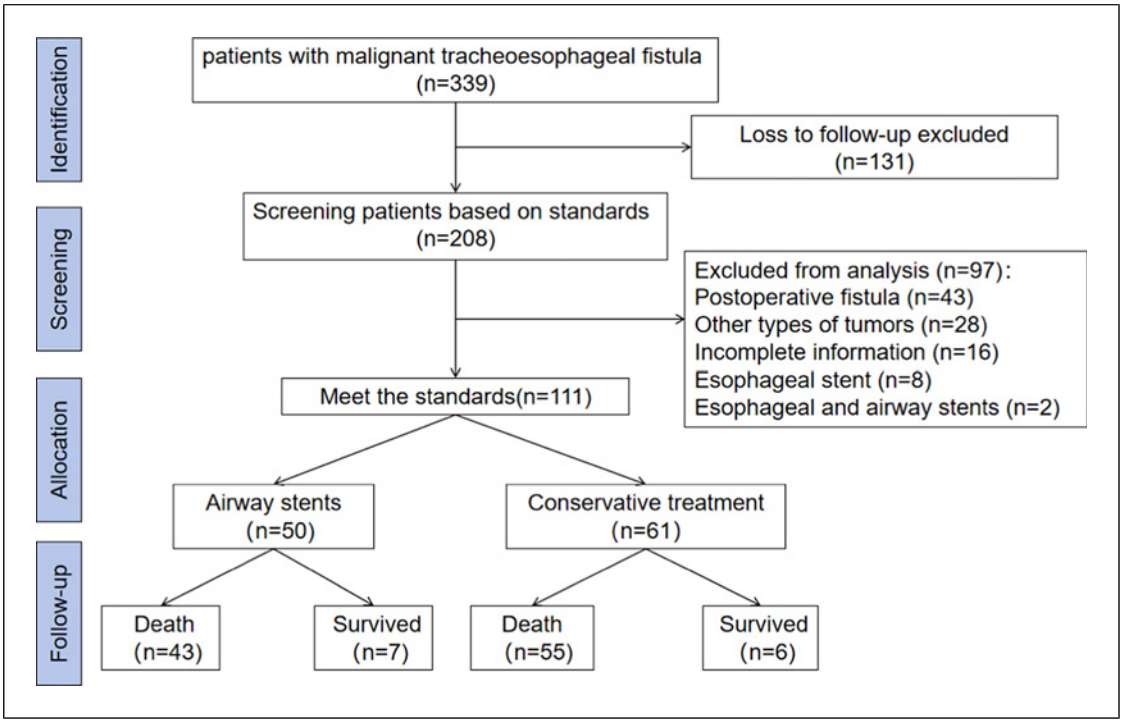

Fig. 1. Flowchart of patient screening.

recorded. To ensure accuracy, all data were cross-referenced with the hospital's electronic medical records. Patient survival, which was calculated from the date of AEF diagnosis to either death or the last available follow-up, constituted the primary endpoint of this study. The incidence of complications and improvements in the quality of life following treatment were the secondary endpoints.

Quality of Life Assessment

Quality of life was assessed using the KPS score, a well-known metric in oncology for quantifying patients' functional impairment. The KPS scale ranges from 0 to 100, with higher scores indicating improved functionality and lower scores reflecting severe disability or dependence. In this study, KPS assessments were conducted before and after treatment, emphasizing on changes in scores following intervention. This approach facilitated a detailed evaluation of how treatments affected patients' daily functioning and overall well-being.

Regarding the stent placement cohort, KPS scores were recorded immediately before stent insertion and during follow-up visits after treatment. Conversely, the conservative treatment group underwent KPS assessments at regular intervals throughout their follow-up care. Changes in KPS scores served as a proxy for measuring the effectiveness of airway stent placement, not only in prolonging survival but also in enhancing the quality of life by alleviating symptoms, including dyspnea, chest pain, and recurrent infections. Key indicators of successful treatment included statistically significant improvements in the KPS scores. Additionally, patient-reported outcomes related to symptom relief and overall comfort were collected through structured interviews when available, further enriching treatment efficacy evaluation.

Statistical Analysis

Data analysis was performed using Statistical Package for the Social Sciences (version 27, IBM, Armonk, NY, USA). To summarize patient demographics and clinical characteristics, descriptive statistics, including means, standard deviations, and proportions, were employed. To compare the stent and conservative treatment groups, independent *t* tests or nonparametric tests were used for continuous variables, whereas chi-square tests were applied for categorical variables. Furthermore, survival analysis was performed using the Kaplan-Meier method to estimate the median survival time. Cox regression analysis was employed for analyzing the independent risk factors.

Table 1. Comparison of clinical characteristics: conservative treatment group versus stent treatment group in patients diagnosed with malignant esophagotracheal fistula

Clinical characteristics	Airway stent group (n = 50)	Conservative care group (n = 61)	p value
Age, years	65.5±9.3	70.1±9.1	0.010
Gender (%)			0.516
Male	38 (76.0%)	43 (70.5%)	
Female	12 (24.0%)	18 (29.5%)	
Smoking (%)			0.796
Yes	25 (50.0%)	29 (47.5%)	
No	25 (50.0%)	32 (52.5%)	
Tumor stage (%)			0.653
T0–T3	34 (68.0%)	39 (63.9%)	
T4	16 (32.0%)	22 (36.1%)	
Primary tumor location (%)			0.091
Neck/upper	24 (48.0%)	24 (39.3%)	
Middle	19 (38.0%)	34 (55.7%)	
Lower	7 (14.0%)	3 (5%)	
Localization of fistula in airway (%)			0.612
Trachea	27 (54.0%)	36 (59.0%)	
Left main bronchus	9 (18.0%)	14 (23.0%)	
Right main bronchus	12 (24.0%)	10 (16.4%)	
Multiple sites	2 (4.0%)	1 (1.6%)	
Tumor treatment (%)			0.707
Surgery	23 (46.0%)	25 (41.0%)	
Radiotherapy	22 (44.0%)	22 (36.1%)	
Chemotherapy	31 (62.0%)	32 (52.5%)	
Immunity	12 (24.0%)	7 (11.5%)	
Pulmonary infection (%)			0.636
Yes	34 (68.0%)	44 (72.1%)	
No	16 (32.0%)	17 (27.9%)	
Fistula size, cm	1.72 (0.70, 2.45)	1.97 (0.73, 2.88)	0.310
Pre-KPS	48.2 (30.0, 62.5)	43.6 (30.0, 60.0)	0.244

For quantitative data that adheres to a normal distribution, the outcomes are presented in the form of mean ± standard deviation. Conversely, when the data deviate from a normal distribution, the median and IQR are employed. Categorical data, on the other hand, are represented using percentages.

Results

Among the 111 patients diagnosed with esophageal cancer-associated AEF, 98 died, and 13 remained alive in the last clinical care record. The majority were males (73.0%), with a mean age of 68 years. Fifty (45.0%) and sixty-one (55.0%) patients received airway stent placement and conservative care, respectively (Table 1). Regarding clinical characteristics, a significant difference in age was noted between the two groups (p = 0.01); however, age and survival time showed no significant correlation (p = 0.418).

The overall mean survival time for the cohort was 147.4 days; however, significant differences were noted between the two treatment groups. Patients who underwent stent placement had a significantly longer mean survival time (192.5 [95% CI, 151.2–233.7] days) than those conservatively treated (110.0 [95% CI, 88.1–131.8] days) (p < 0.001) (Fig. 2).

We analyzed the independent risk factors for survival time in all patients. Male sex (p = 0.017), late tumor stage (p = 0.030), pulmonary infection (p < 0.001), and large fistula (p < 0.001) were identified as the independent risk factors predicting reduced survival time. Meanwhile,

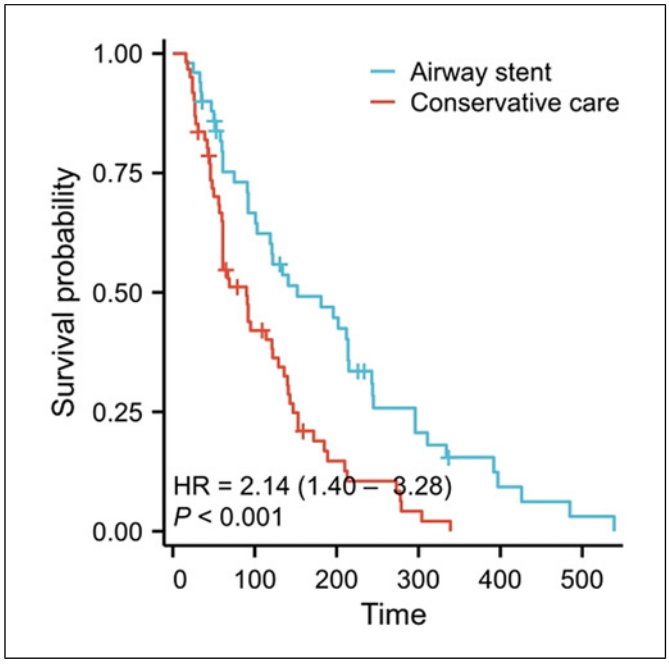

Fig. 2. Kaplan-Meier curves in survival time (days) between conservative treatment group (n = 61) and air stent treatment group (n = 50). Statistical analysis via log-rank tests revealed a significant difference ($p < 0.001$) between the use of air stents and conservative care.

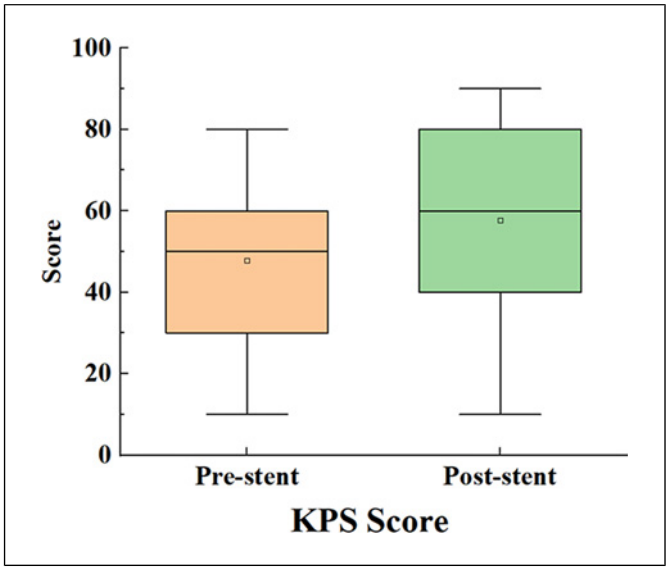

Fig. 3. Analysis of KPS scores. The box plot shows the mean KPS scores for questions pre-stent and post-stent insertion (p = 0.017). Boxes represent median and interquartile range (IQR), and whiskers represent ±1.5 IQR.

previous surgery (p = 0.005) and high pre-KPS ($p < 0.001$) were the independent risk factors prolonging survival time.

Fifty patients with AEF underwent airway stent placement, including 30 who received tract-covered metal stent and 18 who received silicone stent; the stent type did not significantly affect the survival time of patients (p = 0.978). Considering the small sample size, 2 patients who underwent double stent implantation of a tract-covered metal stent combined with a silicone stent were excluded from the analysis.

Furthermore, the KPS scores, which assess patients' functional status, significantly improved in the stent placement group, increasing from 48.2 pre-treatment to 57.9 post-treatment (p = 0.017) (Fig. 3). This enhancement indicates better overall health and functionality following the intervention.

However, 36 patients (72.0%) in the stent placement group developed complications. The most prevalent complication was chest pain (52.8%), followed by cough (27.8%) and stent displacement (5.6%). Despite these concerns, the benefits of the intervention with respect to survival and quality of life significantly outweighed the associated risks, rendering airway stent placement a feasible treatment alternative for managing AEF in patients with esophageal cancer.

Discussion

Esophageal cancer, a highly aggressive malignancy, is frequently complicated by the development of AEF, a condition that significantly worsens patient prognosis and quality of life [15, 16]. Traditionally, owing to the advanced stage of the disease at diagnosis and the complexity of the fistulous connections, management strategies for AEF have been limited and challenging [17].

In general, patients with malignant AEF have poor physical condition, and most of them are poor candidates for surgery [10, 18, 19]. Furthermore, surgery has been hindered by high morbidity and mortality rates, particularly in patients with advanced disease [20]. Currently, majority of these patients are treated with either interventional or conservative treatments. Conservative treatment, including nutritional support and symptomatic treatment, imposes lower physical demands; however, its effect in prolonging survival or improving the quality of life is limited [21].

Owing to recent advances, the focus has shifted toward minimally invasive techniques, with airway stent placement emerging as a promising intervention [22, 23]. This method involves inserting a stent for sealing the fistula and preventing the aspiration of esophageal contents into the airway, thereby reducing severe complications, including aspiration pneumonia and respiratory failure [24]. Airway stent placement offers the benefits of less

surgical trauma, fewer complications, clear curative effect, and treatment is rarely limited by physical conditions [8]. Airway stent placement is a feasible and sufficient intervention for patients with poor physical condition, unsuitable for surgery, or unwilling to undergo surgery.

Furthermore, the economic status of several patients and families may influence the choice of treatment [25]. However, the cost of stents has significantly decreased. Simultaneously, medical insurance can reimburse the cost of stents, which substantially reduces the economic burden of patients.

Although significant differences were noted in terms of age among the clinical characteristics, we observed no significant relationship between age and survival time through Cox regression, which is consistent with previous research findings [26, 27]. Subsequently, considering the large age difference, we conducted a matching analysis, and the results confirmed the conclusion. Therefore, we believe that age is unlikely to affect the survival time of patients, thereby affecting our experimental results.

The key findings of this study highlight the clinical significance of airway stent placement as a therapeutic modality for patients with esophageal cancer-associated AEF. The mean survival time of 192.5 days in the stent placement group significantly surpasses the 110.0 days observed in the conservative treatment group. This finding aligns with previous studies that have indicated the efficacy of airway stents in prolonging survival in patients with AEF. A study by Chou et al. reported similar outcomes, where stent placement was associated with extended survival in patients with advanced esophageal malignancies [28]. The ability of stents to effectively seal the fistula and prevent the aspiration of esophageal contents may be a critical factor contributing to the improved survival outcomes observed in our cohort.

Meanwhile, certain influencing factors can influence the survival time of patients. The reason why late tumor stage, pulmonary infection, and large fistula size are worse than the other groups remains unclear. As these risk factors may make it difficult for the fistula to spontaneously heal, eventually leading to respiratory complications and death, prompt risk stratification and diagnostic efforts are required [7]. Meanwhile, patients with high pre-KPS and had previous surgery frequently have a longer survival period, possibly attributed to their superior physical condition. Notably, following the occurrence of a fistula in patients with esophageal cancer, the average life expectancy of females is longer than that of males. Previous studies have also reported similar results, which may be partially attributed to the general survival advantage of females over males due to the influence of hormones on inflammation and immune responses [9]. To further investigate this phenomenon, future research may be necessary.

Of the 50 patients who underwent airway stent placement, the majority received a tract-covered metal or silicone stents. Both stent types effectively occluded the fistulas, thereby improving the patients' quality of life. The tract-covered metal stent exhibits better adhesion to the airway walls, which can reduce the incidence of migration [11]. However, the tract-covered metal design has a relatively low durability, rendering it prone to metal fatigue and stent fracture [10]. In contrast, silicone stents provide greater durability; however, the shortcoming is that the bolts on the exterior surface of the silicone stent may hinder complete adhesion within the airway lumen, thereby diminishing the stent's sealing efficacy [29].

By mechanically sealing the fistula, the stent effectively curtails the aspiration of esophageal contents into the respiratory tract, thereby mitigating the risk of infections, enhancing respiratory function, and ultimately extending patient survival [30]. The positive impact of stent placement on patients' overall quality of life is highlighted by the marked improvement in KPS scores [31]. In our study, the therapeutic benefit of this intervention is further underscored by the statistically significant improvement in KPS scores from 48.2 to 57.9 following stent placement. This improvement in KPS scores indicates enhanced functionality and a better quality of life, which are frequent critical considerations in managing patients with terminal illnesses.

Despite the notable stent placement-associated benefits, acknowledging the complications reported in our study is critical. With 72.0% of patients in the stent placement group experiencing adverse events, including chest pain, respiratory failure, and stent displacement, careful patient selection and monitoring are paramount. Previous studies have documented these complications, suggesting that although stenting is effective, it is not without risks. Therefore, a multidisciplinary approach is essential in AEF management, integrating the insights of surgical oncologists, interventional pulmonologists, and palliative care specialists for optimizing patient outcomes while minimizing complications.

Although patients with AEF remain to have poor prognoses, the significant disparity between the stent placement group and those undergoing conservative treatment underscores the potential of stent placement as a standard-of-care intervention for these patients [7, 32, 33]. However, acknowledging that stent placement is not devoid of complications is imperative. The prevalence of chest pain and other post-procedural sequelae highlights the invasive nature of this procedure, necessitating vigilant monitoring for managing these complications. Furthermore, stent displacement is not an uncommon occurrence; it can

precipitate critical situations, emphasizing the need for further research into refining stent design and placement techniques for mitigating such incidents.

Limitations and Future Directions

This study had some limitations. The retrospective design may introduce biases, and the relatively small sample size may affect the generalizability of our findings. Furthermore, the analysis of complications relied on clinical documentation, which may not capture all the adverse events experienced by the patients. Future endeavors should include larger patient cohorts and longer follow-up durations to corroborate these findings and delve into potential advancements in stent technology.

Esophageal stents are also an effective tool for fistula closure and AEF treatment; however, for malignant esophageal stent AEF treatment, they may be a risk factor for fistula deterioration, hindering further endoscopic treatment and ideal therapeutic effect [34–36]. Therefore, for malignant AEF, an airway stent may be a better choice. Furthermore, in our study, the number of cases using esophageal stent implantation was relatively small, which may be due to the regional differences in clinical practice affecting treatment choices [37–40]. To explore the long-term efficacy and safety of esophageal stents, subsequent studies with larger sample sizes are warranted.

Furthermore, a multifaceted treatment paradigm integrating stent placement alongside additional therapeutic measures, including chemotherapy or immunotherapy, may yield further improvements in patient outcomes. This study serves as a cornerstone for future investigations into optimal management strategies for AEF in patients with esophageal cancer, with the overarching goal of augmenting survival rates and quality of life.

Conclusion

Airway stent placement has emerged as a secure and efficacious therapeutic approach for managing patients with esophageal cancer-associated AEF. This method prolongs survival time while enhancing the quality of life by effectively sealing the fistula and mitigating respiratory complications. Future large-scale studies are indispensable to further substantiate these observations.

Statement of Ethics

The study was conducted in accordance with the amended Declaration of Helsinki and was approved by the Ethics Committee. This study protocol was reviewed and approved by the Ethics Committee of Henan Provincial People's Hospital, Approval No. 2024(194). Written informed consent was obtained from all participants for the publication of their medical case details.

Conflict of Interest Statement

Prof. Dr. Felix J. Herth was a member of the journal's Editorial Board at the time of submission. The authors declare no conflict of interest.

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Author Contributions

X.N.L., P.Y.L., F.J.H., and Q.C.Z. are involved in the conception and design of the study. X.N.L., P.Y.L., M.Y.Z., F.F.W., G.C.J., Y.B.Y., Y.R.L., and X.W. were involved in the data collection of the study. X.N.L. and P.Y.L. were involved in the analysis and interpretation of the results. P.Y.L. wrote the first draft of the manuscript. All the authors edited, reviewed, and approved the final version of the manuscript.

Data Availability Statement

The original contributions presented in the study are included in the article. Further inquiries can be directed to the corresponding author.

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