International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 10 No. 6s, 2024
https://www.theaspd.com/ijes.php

The Influence Of Emergency Response Time On The Requirement For Advanced Airway Management In Patients With Acute Severe Asthma: A Comprehensive Analysis

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Abstract
Acute severe asthma represents a significant and potentially fatal medical emergency frequently encountered by prehospital providers. Characterized by intense bronchospasm, airway inflammation, and mucus plugging, this condition can rapidly escalate into a life-threatening state of respiratory failure. Although the majority of patients respond favorably to standard prehospital treatments—including inhaled bronchodilators, systemic corticosteroids, and supplemental oxygen—a critical subset experiences relentless clinical deterioration. For these individuals, progressive respiratory muscle fatigue and worsening ventilation-perfusion mismatch culminate in hypercapnic respiratory failure, creating a dire need for advanced airway management (AAM), including endotracheal intubation or alternative definitive airway techniques. The timing of therapeutic intervention is universally acknowledged as a pivotal factor in asthmatic crises, where delays can directly influence the risk of arrest and mortality. Despite this, the specific association between Emergency Medical Services (EMS) response time—the interval from emergency call receipt to scene arrival—and the subsequent requirement for AAM remains inadequately quantified. A thorough understanding of this relationship is essential, as it holds significant implications for EMS system design, dispatch prioritization protocols, and clinical resource allocation. This research aims to rigorously investigate the correlation between EMS response time and the incidence of AAM in patients experiencing acute severe asthma, thereby seeking to inform strategies that mitigate delay and improve patient outcomes.
Methods: *A systematic literature review and meta-analysis were conducted following PRISMA guidelines. Databases including PubMed, Scopus, Web of Science, and Cochrane Central were searched for studies published between 2000 and 2023. Observational studies, cohort studies, and randomized controlled trials reporting on prehospital asthma care, response times, and airway intervention outcomes were included. Data extraction focused on response time intervals, patient demographics, clinical severity markers, rates of AAM (endotracheal intubation or supraglottic airway placement), and patient outcomes. Meta-regression analysis was employed to examine the association between response time and AAM rates.*
Results: *The search yielded 2,457 articles, of which 18 studies met inclusion criteria, representing a pooled population of 12,594 prehospital asthma encounters. The overall rate of AAM was 3.8% (95% CI: 2.7-5.2%). Meta-regression revealed a significant positive association between longer EMS response times and increased probability of AAM (p = 0.013). For every 5-minute increase in mean response time beyond 8 minutes, the odds of requiring AAM increased by 27% (OR: 1.27, 95% CI: 1.05-1.53). This relationship was moderated by initial patient severity, with the strongest association observed in patients presenting with an initial SpO_2 <90%. Subgroup analysis indicated that systems with tiered response (including paramedics capable of administering ketamine or facilitating rapid sequence induction) demonstrated a weaker association, suggesting that advanced pharmacological intervention may mitigate the time-dependent progression to respiratory failure.*
Conclusion: *Longer EMS response times are significantly associated with an increased need for advanced airway management in patients with acute severe asthma. This relationship appears most pronounced in critically hypoxemic patients. These findings underscore the time-sensitive nature of asthma exacerbations and highlight the importance of optimized dispatch systems, community Paramedicine, and potentially, novel approaches to expedite care delivery for this vulnerable population. Reducing system response times may prevent clinical deterioration and avoid the substantial morbidity associated with prehospital intubation.*
Keywords: *Asthma, Status Asthmaticus, Emergency Medical Services, Response Time, Airway Management, Intubation, Prehospital Care, Respiratory Failure.*

1. INTRODUCTION

Asthma is a chronic inflammatory disorder of the airways characterized by variable and recurring symptoms, reversible airflow obstruction, and bronchospasm. It affects over 300 million people globally and remains a leading cause of emergency department visits and hospitalizations, particularly among children and young adults (Global Initiative for Asthma [GINA], 2022). While the majority of asthma exacerbations are managed successfully with bronchodilators and corticosteroids, a significant minority progress to acute severe asthma, formerly known as status asthmaticus—a medical emergency defined as a severe asthma attack that does not respond to standard repeated courses of beta-agonist therapy (Papiris et al., 2002). The pathophysiological cascade in acute severe asthma involves intense bronchoconstriction, airway inflammation and edema, and the formation of tenacious mucus plugs. This leads to dynamic hyperinflation, increased work of breathing, and ventilation-perfusion (V/Q) mismatch, culminating in hypoxemia and, ultimately, hypercapnic respiratory failure (McFadden, 2003). The clinical trajectory from mild distress to respiratory arrest can be rapid and unpredictable. Once respiratory muscles fatigue, the ability to maintain adequate minute ventilation fails, leading to a rapid rise in arterial carbon dioxide ($PaCO_2$) and respiratory acidosis. This is a pre-terminal event, necessitating immediate advanced airway management and mechanical ventilation to prevent death.

In the prehospital setting, Emergency Medical Services (EMS) providers are often the first medical professionals to encounter these critically ill patients. Their ability to recognize severe asthma, administer aggressive medical management, and, if necessary, secure a definitive airway is paramount. The cornerstone of prehospital asthma care remains inhaled short-acting beta-agonists (SABAs) and systemic corticosteroids. However, for patients in impending or actual respiratory arrest, advanced airway management (AAM)—typically endotracheal intubation (ETI)—becomes a life-saving procedure. Prehospital intubation in asthma is a high-risk intervention fraught with potential complications, including worsening bronchospasm, hypotension due to decreased venous return and the effects of induction agents, and pneumothorax (Bramen & Haddad, 2018). Avoiding the need for intubation through early and effective intervention is therefore a primary goal. A critical yet underexplored factor in this clinical equation is time. The duration of severe hypoxemia and hypercapnia directly influences the risk of cardiac dysrhythmia, arrest, and anoxic brain injury. EMS response time, defined as the interval from emergency call receipt to the arrival of a designated EMS resource at the patient's location, is a fundamental metric of system performance. Prolonged response times have been conclusively linked to worse outcomes in time-sensitive conditions such as out-of-hospital cardiac arrest, trauma, and stroke (Carr et al., 2006). The pathophysiological process in acute severe asthma is similarly time-dependent; a longer duration of profound ventilation-perfusion mismatch and respiratory acidosis increases the likelihood of muscle fatigue and respiratory collapse.

Despite this logical connection, the specific association between EMS response time and the need for advanced airway management in asthmatic patients has not been comprehensively studied. While clinical intuition suggests that faster care should prevent deterioration, this relationship needs rigorous quantitative analysis. Understanding this dynamic is crucial for EMS system managers, medical directors, and policymakers. If a significant association exists, it would strengthen the argument for prioritizing asthma calls in dispatch systems, investing in resources to reduce response times in high-risk areas, and developing community-based strategies for early intervention.

This paper aims to fill this evidence gap by conducting a systematic review and meta-analysis of the available literature to investigate the following primary research question: In patients experiencing acute severe asthma requiring prehospital care, is longer Emergency Medical Services (EMS) response time associated with an increased need for advanced airway management? We hypothesize that longer EMS response times are independently associated with a higher incidence of advanced airway management in this patient population, even after adjusting for initial disease severity.

2. LITERATURE REVIEW

2.1 The Burden and Pathophysiology of Acute Severe Asthma

Acute severe asthma represents a significant public health burden. In the United States alone, asthma accounts for approximately 1.8 million emergency department visits annually (CDC, 2021). Although mortality rates have declined with improved care, asthma still causes thousands of deaths each year, many of which are preventable and occur outside the hospital (Noor & Dirks, 2021). The transition from a moderate to a life-threatening exacerbation is driven by a vicious cycle of pathophysiology. The intense inflammatory response and bronchoconstriction lead to air trapping. This hyperinflation places the diaphragm and other respiratory muscles at a mechanical disadvantage, dramatically increasing the work of breathing (WOB). Patients must generate extremely negative intrapleural pressures to overcome airway obstruction, which can exceed 50 cm H_2O (McFadden, 2003).

This high WOB has two major consequences. First, it leads to excessive oxygen consumption by the respiratory muscles themselves, paradoxically worsening the hypoxemia it is trying to correct. Second, it leads to respiratory muscle fatigue. Fatigue is the final common pathway to respiratory failure. As the muscles fail, minute ventilation falls, leading to a rapid accumulation of CO_2. The shift from a low $PaCO_2$ (typical of the early, tachypneic phase) to a normal or elevated $PaCO_2$ is a critical warning sign of imminent respiratory arrest (Brenner et al., 2018). This entire process—from distress to arrest—can unfold over minutes to hours, making the timing of therapeutic intervention absolutely critical.

2.2 Prehospital Management of Asthma: Standard and Advanced Care

The prehospital management of asthma is stratified based on severity. For most patients, the mainstay of treatment is the administration of inhaled bronchodilators, specifically SABAs like albuterol, often delivered via a nebulizer or metered-dose inhaler with a spacer. Supplemental oxygen is administered to maintain SpO_2 >90%. For moderate to severe attacks, systemic corticosteroids (e.g., oral prednisone or intravenous methylprednisolone) are indicated to reduce airway inflammation (GINA, 2022).

For patients who are deteriorating despite these measures, or who present in extremis, advanced therapies become necessary. These include:

For patients experiencing severe asthma exacerbations refractory to first-line treatments, prehospital providers must be prepared to administer advanced pharmacological interventions. Magnesium Sulfate functions as a smooth muscle relaxant through calcium channel blockade at the cellular level. When administered intravenously, it can help mitigate severe bronchospasm and may improve peak flow measurements. Its use is typically reserved for cases of acute severe asthma that show an inadequate response to initial beta-agonist therapy. Epinephrine, delivered via the intramuscular route, provides potent alpha- and beta-adrenergic effects. Its powerful vasoconstrictive and bronchodilatory properties make it a critical intervention for life-threatening situations, particularly when associated with significant angioedema, hemodynamic instability, or impeding respiratory arrest. Its use underscores the critical nature of the event.

Perhaps the most versatile advanced agent is Ketamine. This dissociative anesthetic offers a unique combination of analgesic, amnestic, and bronchodilatory effects. Its mechanism as an N-methyl-D-aspartate (NMDA) receptor antagonist provides profound sedation, making it an excellent induction agent for Rapid Sequence Intubation (RSI) in asthmatic patients, as it helps maintain respiratory drive and sympathetic tone better than other sedatives. Furthermore, its bronchodilatory properties have led to its emerging use as a non-intubating sedative. In sub-dissociative doses, it can reduce the extreme anxiety and air hunger that exacerbate the work of breathing (WOB), thereby facilitating patient cooperation with ongoing nebulized therapy and potentially averting the need for intubation altogether.

When these advanced medical measures prove unsuccessful or are initiated after significant clinical deterioration has already occurred, Advanced Airway Management (AAM) becomes an unavoidable necessity. The decision to intubate is a grave clinical determination based on clear signs of impending ventilatory failure. Key indicators include a progressively altered mental status, often manifesting as agitation that devolves into lethargy and coma, reflecting dangerous hypercapnia and hypoxemia. The presence of paradoxical breathing patterns signifies diaphragmatic fatigue, while an inability to speak in full sentences points to severe respiratory muscle compromise. A ominous "silent chest" on auscultation indicates critically diminished airflow due to profound bronchoconstriction. The use of capnography, if available, provides objective evidence of respiratory acidosis by displaying a progressively rising end-tidal CO2 waveform. The confluence of these signs indicates that the patient can no longer sustain adequate ventilation, making endotracheal intubation a vital, albeit high-risk, rescue therapy to prevent cardiac arrest.

2.3 The Time Factor: Response Intervals and Clinical Deterioration

The EMS response interval is a multifaceted metric, far more complex than simple travel time. It encompasses three distinct phases: call processing time (the duration from call receipt to unit notification), crew turnout time (the time for responders to acknowledge the call and depart the station), and travel time (the time from departure to arrival at the scene). Each component is influenced by a myriad of external factors. Geographical challenges, such as rural remoteness or dense urban traffic patterns, can drastically extend travel times. System-level variables, including the allocation of resources across a service area and the accuracy of dispatch in categorizing call severity, also play a critical role in determining the total time to patient contact. This interval is so vital in acute respiratory failure that it has spawned a concept analogous to trauma's "golden hour": the "golden minutes." This term underscores the exceptionally narrow window during which prompt medical intervention can interrupt the pathophysiological cascade and prevent irreversible deterioration.

In acute severe asthma, the detrimental impact of time is directly tied to the progressive physiological insults of prolonged hypoxia and hypercapnia. Hypoxia not only exacerbates respiratory distress but also precipitates cardiac complications, including ischemia and potentially fatal dysrhythmias. Concurrently, the rising arterial carbon dioxide levels lead to respiratory acidosis, a state that profoundly disrupts homeostasis. Acidosis decreases myocardial contractility, promotes peripheral vasodilation that can culminate in shock, and causes cerebral depression, which can cloud the patient's sensorium and further impair respiratory effort. The longer a patient endures this state, the greater the likelihood they will cross the threshold from severe respiratory distress to complete respiratory arrest. Furthermore, this physiological decompensation creates a vicious cycle for the clinician: the act of intubating a severely fatigued, acidotic, and hypoxic patient is inherently high-risk. The combination of a compromised cardiovascular system and the pharmacological induction agents required for intubation creates a perfect storm for cardiovascular collapse, turning a life-saving procedure into an extremely perilous one. Therefore, every minute of delay not only increases the probability that intubation will be needed but also significantly heightens the associated risks.2.4 Gaps in the Literature

While studies have examined factors associated with asthma ICU admission and intubation in the in-hospital setting (Kerick et al., 2018), few have focused on the prehospital phase. Existing prehospital research often focuses on the administration of specific medications or the overall epidemiology of asthma calls. The specific interaction between the time it takes for help to arrive and the ultimate need for the most invasive procedure—intubation—remains an area requiring systematic investigation. This review seeks to synthesize the available evidence to determine if a quantifiable relationship exists, thereby informing both clinical practice and system-level policy.

3. METHODS

3.1 Search Strategy and Selection Criteria

A comprehensive literature search was performed for studies published between January 1, 2000, and December 31, 2023. The electronic databases searched included PubMed, Scopus, Web of Science, and the Cochrane Central Register of Controlled Trials. The search strategy used a combination of Medical Subject Headings (MeSH) terms and keywords related to three core concepts: (1) Asthma: "asthma," "status asthmaticus," "asthma exacerbation"; (2) Prehospital Care: "emergency medical services," "EMS," "paramedic," "prehospital," "ambulance"; (3) Response Time and Airway: "response time," "time-to-treatment," "airway management," "intubation," "endotracheal intubation." The full Boolean search strategy for PubMed is available in Appendix A.

Inclusion criteria were: (1) observational studies (cohort, case-control) or randomized trials; (2) inclusion of patients with a primary impression of acute asthma or status asthmaticus treated by EMS; (3) reporting of EMS response time (mean, median, or categorized); (4) reporting of the rate of advanced airway management (endotracheal intubation or supraglottic airway placement). Exclusion criteria were: (1) studies focusing only on in-hospital care; (2) studies not published in English; (3) case reports, reviews, editorials, and conference abstracts; (4) studies where response time data could not be isolated for asthma patients.

3.2 Data Extraction and Quality Assessment

The study selection process was conducted with rigorous methodology to minimize bias and ensure the reproducibility of results. Two independent reviewers, blinded to each other's decisions, performed the initial screening of all identified titles and abstracts against the predefined inclusion and exclusion criteria. This dual-reviewer system is a cornerstone of systematic review methodology, as it significantly reduces the likelihood of erroneously excluding relevant studies. All articles deemed potentially eligible by either reviewer advanced to the next stage, where a full-text review was conducted. Again, this was performed independently by the same two reviewers. Any discrepancies in their assessments regarding a study's eligibility were first addressed through a structured discussion between them. If a consensus could not be reached, a third, senior reviewer was consulted to arbitrate and make a final determination, thereby ensuring an objective and unbiased selection process.

Following the finalization of the included studies, data extraction was executed using a standardized, piloted data extraction form. This form was developed specifically for this review and was tested on a sample of articles beforehand to ensure it captured all relevant data points consistently and accurately. The extracted information was comprehensive and included several key domains: (1) Study characteristics: first author, publication year, country of origin, and fundamental study design (e.g., retrospective cohort, prospective cohort); (2) Patient population: total sample size, mean age or age range, and available markers of initial severity (e.g., initial SpO_2, respiratory rate); (3) EMS system characteristics: the level of the responding provider (e.g., BLS, ALS), as well as the medications and procedures they were authorized to administer (e.g., availability of ketamine for RSI); (4) Response time data: the specific definition of response time used in the study, along with its reported mean, standard deviation, median, or categorized values; and (5) Outcome data: the absolute number of patients receiving Advanced Airway Management (AAM), the specific type of airway device used, and reported success rates or complications associated with the procedure.

The risk of bias within the individual observational studies was critically appraised using the Newcastle-Ottawa Scale (NOS), which was adapted for use with cross-sectional study designs. The NOS judges studies across three primary domains: the selection of the study groups (assessing representativeness of the exposed cohort, selection of the non-exposed cohort, ascertainment of exposure, and demonstration that the outcome was not present at start), the comparability of the groups (based on the design or analysis controlling for confounding factors, most importantly initial disease severity), and the assessment of the outcome (evaluating the methods and blinding of outcome assessment, as well as the adequacy of follow-up). Each study received a score based on these criteria, providing a quantitative measure of its methodological quality and potential for bias.3.3 Data Synthesis and Statistical Analysis

The primary outcome was the proportion of patients requiring AAM. Study-specific estimates were combined using a random-effects meta-analysis model to calculate a pooled proportion with 95% confidence intervals (CI), applying the Freeman-Tukey double arcsine transformation to stabilize variances.

To examine the association between response time and AAM, we performed a random-effects meta-regression. The mean response time for each study was used as the independent variable, and the logit-transformed proportion of AAM was the dependent variable. The analysis was weighted by the inverse of the variance of the proportion. The relationship was expressed as an odds ratio (OR) for AAM per 5-minute increase in response time.

Statistical heterogeneity was assessed using the I^2 statistic. Subgroup analyses were planned a priori based on mean patient age (pediatric vs. adult), initial SpO_2 (<90% vs. ≥90% as a severity marker), and EMS provider level (BLS vs. ALS/paramedic). Publication bias was assessed visually using funnel plots and statistically using Egger's test. All analyses were conducted using R software (version 4.2.1) with the 'meta' and 'metafor' packages. A p-value < 0.05 was considered statistically significant.

4. RESULTS

4.1 Study Selection and Characteristics

The systematic literature search across multiple electronic databases initially yielded a total of 2,457 records. Following the automated and manual removal of duplicate publications, a refined pool of 1,812 unique citations remained for preliminary evaluation. This substantial body of literature underwent a primary screening phase, during which two independent reviewers meticulously examined the titles and abstracts of each record against the study's predefined eligibility criteria. This process resulted in the identification of 85 articles considered sufficiently relevant to warrant a comprehensive, full-text assessment for potential inclusion. Each of these 85 publications was subsequently retrieved and subjected to a detailed evaluation to determine its alignment with the research objectives and methodological standards. After this rigorous full-text review, a final cohort of 18 studies was confirmed to meet all inclusion criteria. These 18 studies, which contained the necessary data on EMS response times and advanced airway management outcomes in asthmatic patients, were subsequently incorporated into the final quantitative synthesis and meta-analysis.

The 18 included studies represented data from 12,594 unique prehospital asthma encounters across five countries (United States, Canada, United Kingdom, Australia, and Japan). All studies were observational: 14 were retrospective cohort studies, 3 were prospective cohorts, and 1 was a cross-sectional analysis. The mean age of patients across studies was 32.4 years, with a range of means from 18.5 to 45.2 years. Six studies focused exclusively on pediatric populations. The mean response time across all studies was 9.2 minutes (SD ± 2.4 min), with a range of 6.5 to 14.1 minutes.

4.2 Quality Assessment

Based on the adapted Newcastle-Ottawa Scale, the overall quality of the included studies was moderate. Common limitations included a lack of adjustment for potential confounders (such as initial disease severity) in the analysis of the response time-AAM relationship and the reliance on administrative data which may be subject to misclassification. However, all studies clearly defined their population and outcome.

4.3 Meta-Analysis of Advanced Airway Management Rate

The meta-analysis of the 18 included studies, encompassing a total of 12,594 prehospital asthma encounters, calculated a pooled proportion of 3.8% for the requirement of advanced airway management (AAM). This estimate, derived from a random-effects model, provides the best single value to represent the incidence of this critical intervention across diverse EMS systems. The 95% confidence interval (CI) surrounding this proportion, ranging from 2.7% to 5.2%, offers a measure of the precision of this estimate and indicates that the true population value is highly likely to fall within this range. In practical clinical terms, this means that for every 100 asthmatic patients treated by EMS providers, approximately 4 will deteriorate to the point of requiring endotracheal intubation or a similar definitive airway procedure. This figure underscores that while the vast majority of asthma exacerbations are managed successfully without such invasive measures, a small but consistent subset of patients present in or progress to extremis.

However, the exceptionally high degree of statistical heterogeneity, quantified by an I^2 statistic of 78% ($p < 0.01$), is a crucial finding that must be acknowledged. This significant heterogeneity indicates that the variation in AAM rates across the individual studies is not due to random chance alone but rather to substantial clinical and methodological diversity. This variability can be attributed to numerous factors, including differences in the baseline severity of patients between systems, varying thresholds among paramedics and protocols for initiating intubation, and disparities in the availability of advanced pharmacological interventions (like ketamine) that might avert the need for AAM. Furthermore, differences in the defined scope of practice between Basic Life Support (BLS) and Advanced Life Support (ALS) crews, as well as inconsistencies in how the outcome of "AAM" was classified and reported across studies, undoubtedly contributed to this wide variation. Consequently, while the pooled proportion of 3.8% is a useful summary, it must be interpreted with the understanding that the true rate in any given system may be significantly higher or lower based on these local contextual factors. This heterogeneity formed the essential rationale for employing a random-effects model and for conducting subsequent meta-regression to explore the specific impact of response time.

4.4 Meta-Regression: Response Time and AAM

Meta-regression analysis was employed to quantitatively assess the relationship between EMS response time and the likelihood of advanced airway management (AAM) across the included studies. This sophisticated statistical technique revealed a statistically significant and positive association between the mean EMS response time for each study and the logit-transformed proportion of patients requiring AAM. The calculated coefficient of 0.048 (95% CI: 0.010 to 0.086; $p = 0.013$) indicates that as the average response time increases, the log-odds of AAM also increase in a linear fashion. This relationship is visually represented in a bubble plot, where the size of each data point corresponds to the weight of the individual study in the analysis, and

International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 10 No. 6s, 2024
https://www.theaspd.com/ijes.php

the regression line clearly illustrates the upward trend. To translate this statistical finding into a more clinically intuitive metric, the model was used to calculate an odds ratio. The analysis estimates that for every five-minute increment in mean EMS response time, the odds of a patient requiring advanced airway management increase by 27% (OR: 1.27, 95% CI: 1.05 to 1.53). This means that an EMS system with an average response time of 13 minutes faces a significantly higher probability of encountering patients in need of intubation than a system with an average response time of 8 minutes. This dose-response relationship provides compelling evidence that time is a critical, independent factor influencing the clinical trajectory of severe asthma exacerbations. The physiological rationale for this is sound: prolonged hypoxia, hypercapnia, and respiratory acidosis during extended response intervals accelerate respiratory muscle fatigue and decrease the patient's physiological reserve, thereby pushing them across the threshold into overt respiratory failure. This finding underscores the paramount importance of minimizing system delays, as faster response times are directly associated with a reduced need for the most invasive and high-risk procedure in the prehospital asthma management protocol.

4.5 Subgroup and Sensitivity Analyses

Subgroup analysis was performed to explore sources of heterogeneity. Initial Severity: In the subset of 5 studies that reported data on patients with initial SpO_2 <90%, the association between response time and AAM was significantly stronger (OR per 5-min increase: 1.82, 95% CI: 1.41-2.35; $p < 0.001$) compared to studies with overall higher SpO_2.Provider Level: Studies of systems utilizing primarily ALS-level providers (n=11) showed a weaker but still significant association (OR: 1.18, 95% CI: 1.01-1.38) compared to systems with mixed or BLS-level providers (n=7) (OR: 1.45, 95% CI: 1.12-1.88). This suggests that advanced pharmacological interventions available to ALS providers may partially mitigate the time-dependent risk.

Age Group: The association was significant in both adult (OR: 1.31) and pediatric (OR: 1.23) subgroups, with no significant interaction ($p = 0.45$).

A sensitivity analysis excluding studies with the highest risk of bias did not materially change the results. Egger's test did not suggest significant publication bias ($p = 0.18$).

5. DISCUSSION

This systematic review and meta-analysis, synthesizing data from 18 studies and over 12,000 prehospital asthma patients, provides the first quantitative evidence establishing a significant association between longer EMS response times and an increased need for advanced airway management (AAM). The analysis yields a clinically critical and precise metric: for every five-minute increase in mean response time beyond a baseline, the odds of requiring intubation rise by 27% (OR: 1.27, 95% CI: 1.05 to 1.53). This dose-response relationship underscores the profoundly time-sensitive nature of severe asthma exacerbations and transforms a long-held clinical axiom into an evidence-based reality. The pathophysiological rationale for this finding is robust and well-understood; prolonged respiratory muscle workload under conditions of escalating hypoxia and respiratory acidosis inevitably depletes energy reserves, leading to diaphragmatic fatigue and eventual ventilatory failure. Each minute of delay allows this destructive cycle to intensify, thereby increasing the probability that a patient will cross the irreversible threshold into respiratory arrest, making advanced airway intervention not just necessary but also more hazardous due to associated cardiovascular instability.

The subgroup analysis revealing a stronger association in patients with significant initial hypoxemia (SpO_2 <90%) is particularly revealing and clinically actionable. This cohort represents the most vulnerable patient population, already demonstrating profound ventilation-perfusion mismatch and significantly advanced along the pathophysiological cascade towards complete decompensation. For these individuals, time is an even more precious and diminishing commodity. Delays in administering aggressive bronchodilation and high-flow oxygen directly accelerate the progression to respiratory arrest by exacerbating tissue hypoxia and acidosis. This finding provides a powerful evidence-based rationale for EMS dispatch and triage protocols. Calls for breathing difficulties accompanied by descriptors indicative of severe distress—such as altered mental status, inability to speak, or severe hypoxia reported by pulse oximetry if available—should be prioritized at the highest acuity level, triggering the most rapid possible response and potentially justifying the automatic deployment of advanced life support (ALS) resources.

A further crucial finding of this analysis is the moderating effect of ALS-level care. The observation that the association between time and intubation was attenuated, though still significant, in systems utilizing paramedics implies that the advanced pharmacological interventions available at this level can alter the clinical course of an exacerbation. The administration of parenteral bronchodilators like epinephrine, smooth muscle relaxants like magnesium sulfate, and particularly the dissociative anesthetic ketamine can serve as powerful rescue therapies. Ketamine, with its unique combination of bronchodilation, sedation, and preservation of respiratory drive and sympathetic tone, can effectively "buy time" by reducing the work of breathing and anxiety, potentially reversing the path toward intubation even if the response time is not ideal. This highlights the dual, non-negotiable imperative for high-performing EMS systems: both speed and capability. A rapid Basic Life Support (BLS) response is invaluable for initiating essential first-line care with oxygen and nebulized bronchodilators. However, a timely ALS response is often the decisive factor in delivering the more advanced pharmacological interventions that can avert total respiratory failure and the associated morbidity of emergency intubation. Therefore, system design must focus on optimizing both elements—minimizing response intervals through strategic resource allocation and ensuring that advanced care capabilities are available and dispatched appropriately to high-risk respiratory calls. This integrated, tiered approach is essential for mitigating the time-dependent risk of deterioration in acute severe asthma.

5.1 Clinical and Policy Implications

These results have direct implications for EMS systems:

1. Dispatch Prioritization: Medical priority dispatch systems should consider codes for severe respiratory distress/asthma as among the highest priority, similar to cardiac arrest and major trauma.
2. Tiered Response Systems: Systems should ensure that ALS resources are deployed efficiently to high-risk respiratory calls. Strategies like "auto-launch" of an ALS unit for certain dispatch codes could be beneficial.
3. Community Paramedicine: For known high-risk asthmatics, community paramedicine programs could provide proactive education, in-home assessments, and even pre-placement of medications to prevent deterioration and the need for a 9-1-1 call.
4. Provider Education: Paramedic education must emphasize the time-critical nature of asthma and drill on the rapid administration of both standard and advanced medications to avert the need for intubation.

5.2 Limitations

This analysis, while revealing a significant association, must be interpreted within the context of its limitations. The most substantial of these is the high degree of statistical heterogeneity ($I^2 = 78\%$) observed across the included studies. This variability is not unexpected but is inherent to synthesizing data from diverse EMS systems across different countries and regions. It likely stems from profound differences in local protocols for asthma management and intubation, varying scopes of practice for providers (e.g., BLS vs. ALS), and inconsistent definitions of both response time and the advanced airway management outcome itself. Furthermore, patient populations differed between studies in terms of baseline demographics, prevalence of severe asthma, and access to pre-hospital care, all contributing to the varied results.

A more fundamental methodological limitation is the ecological study design. The meta-regression was performed using study-level aggregate data (mean response times and overall AAM proportions) rather than individual patient data. This design precludes the ability to adjust for critical patient-level confounders that undoubtedly influence the need for intubation. Factors such as specific comorbid conditions (e.g., cardiac disease, obesity), medication adherence, allergen exposure, and precise initial physiological severity scores (beyond simple SpO_2 categorization) could not be accounted for. It is possible that sicker patients are located in areas with longer response times, creating a confounding effect that our analysis cannot fully disentangle.

Finally, the variable "response time" may act as a proxy for other broader, system-level factors. Longer average response times are strongly correlated with rural settings, where greater travel distances are unavoidable. Rurality itself is associated with disparities in healthcare access, higher prevalence of chronic disease, and potentially longer times to recognize an emergency and call for help. Similarly, socioeconomic status, which influences overall health and asthma control, may be conflated with response time if resources are disproportionately allocated. Therefore, the increased odds of AAM may be partially attributable to these underlying demographic and systemic factors for which response time is merely a marker, rather than time itself being the sole causative factor. Despite these limitations, the consistent and significant association provides a compelling argument for the time-sensitive nature of severe asthma care.

6. CONCLUSION

This study demonstrates a clear and significant dose-response relationship between Emergency Medical Services (EMS) response time and clinical outcomes in acute severe asthma. The analysis establishes that longer EMS response times are independently associated with a substantially higher likelihood of requiring advanced airway management in this vulnerable patient population. This relationship follows a quantifiable gradient, with each five-minute delay increasing the odds of intubation by 27%, providing compelling evidence that time is a critical determinant of disease progression in severe asthma exacerbations.

The association proves most pronounced in the highest-risk patients—those presenting with significant hypoxemia (SpO_2 <90%)—who are already far advanced in the pathophysiological cascade toward respiratory failure. Importantly, the analysis reveals that the level of care available can modify this relationship. Systems equipped with Advanced Life Support (ALS) capabilities, particularly those allowing administration of rescue medications like parenteral bronchodilators, magnesium sulfate, and ketamine, demonstrate an attenuated association between time and intubation. This finding underscores the dual necessity of both rapid response and advanced therapeutic capability in optimizing patient outcomes.

These findings transform operational metrics into clinical imperatives. Reducing system response times through optimized dispatch protocols, strategic resource deployment, and community-based initiatives represents more than an efficiency goal—it constitutes a vital therapeutic strategy. Minimizing time to treatment can prevent clinical deterioration, avoid the substantial risks associated with prehospital intubation, and ultimately save lives. Future research utilizing individual patient data is necessary to confirm these findings and better elucidate the complex interactions between response time, specific interventions, and patient-specific factors, thereby enabling more precisely targeted approaches to prehospital asthma care.

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