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LONG-TERM FUNCTIONAL AND RESPIRATORY OUTCOMES AFTER ESOPHAGEAL ATRESIA REPAIR: A SYSTEMATIC REVIEW

DESFECHOS FUNCIONAIS E RESPIRATÓRIOS EM LONGO PRAZO APÓS A CORREÇÃO DA ATRESIA DE ESÔFAGO: UMA REVISÃO SISTEMÁTICA

RESULTADOS FUNCIONALES Y RESPIRATORIOS A LARGO PLAZO TRAS LA REPARACIÓN DE LA ATRESIA ESOFÁGICA: UNA REVISIÓN SISTEMÁTICA

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ABSTRACT

Introduction: Esophageal atresia (EA) is a congenital malformation that remains associated with significant long-term morbidity despite improved survival. Post-repair complications such as tracheomalacia, chronic cough, dysphagia, and recurrent respiratory infections can persist throughout life, emphasizing the importance of multidisciplinary and prolonged follow-up.

Objective: To systematically review the available evidence on long-term functional and respiratory outcomes after surgical repair of esophageal atresia, integrating data from recent clinical studies to identify predictors, management strategies, and implications for lifelong care.

Methods: A comprehensive literature search was conducted in PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and ICTRP. Studies from the past five years were prioritized, with extension to ten years if fewer than ten eligible articles were found. Human studies were included; animal and in vitro studies were analyzed separately. Methodological quality was assessed using RoB 2, ROBINS-I, and QUADAS-2, and certainty of evidence was graded with GRADE criteria.

Results and Discussion: Twenty studies met the inclusion criteria. Persistent respiratory morbidity and reduced lung function were observed in most cohorts, regardless of surgical technique. Primary tracheopexy and airway pexy improved airway stability in selected patients. Quality of life assessments demonstrated ongoing functional limitations and psychosocial distress. Evidence heterogeneity was moderate, and certainty ranged from low to moderate. Despite improved perioperative care, the burden of chronic respiratory and gastrointestinal sequelae remains substantial.

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Conclusion: Survivors of esophageal atresia repair frequently experience long-term functional and respiratory complications. Continuous multidisciplinary follow-up, standardized outcome measures, and registry-based research are essential to optimize prognosis and guide individualized management.

Keywords: Esophageal Atresia. Respiratory Function. Long-Term Outcomes. Quality of Life.

RESUMO

Introdução: A atresia de esôfago (AE) é uma malformação congênita que permanece associada a morbidade significativa em longo prazo, apesar da melhoria na sobrevivência. Complicações pós-reparo, como traqueomalácia, tosse crônica, disfagia e infecções respiratórias recorrentes, podem persistir ao longo da vida, ressaltando a importância do acompanhamento multidisciplinar e prolongado.

Objetivo: Revisar sistematicamente as evidências disponíveis sobre os desfechos funcionais e respiratórios em longo prazo após o reparo cirúrgico da atresia de esôfago, integrando dados de estudos clínicos recentes para identificar preditores, estratégias de manejo e implicações para o cuidado ao longo da vida.

Métodos: Foi realizada uma busca abrangente nas bases PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov e ICTRP. Estudos dos últimos cinco anos foram priorizados, com extensão para dez anos caso menos de dez artigos elegíveis fossem encontrados. Estudos em humanos foram incluídos; estudos em animais e in vitro foram analisados separadamente. A qualidade metodológica foi avaliada utilizando RoB 2, ROBINS-I e QUADAS-2, e a certeza da evidência foi graduada pelos critérios GRADE.

Resultados e Discussão: Vinte estudos atenderam aos critérios de inclusão. Morbidade respiratória persistente e redução da função pulmonar foram observadas na maioria das coortes, independentemente da técnica cirúrgica. Traqueopexia primária e pexia das vias aéreas melhoraram a estabilidade aérea em pacientes selecionados. Avaliações de qualidade de vida demonstraram limitações funcionais contínuas e sofrimento psicossocial. A heterogeneidade das evidências foi moderada e a certeza variou de baixa a moderada. Apesar da melhoria no cuidado perioperatório, a carga de sequelas respiratórias e gastrointestinais crônicas permanece substancial.

Conclusão: Sobreviventes do reparo da atresia de esôfago frequentemente apresentam complicações funcionais e respiratórias em longo prazo. Acompanhamento multidisciplinar contínuo, medidas padronizadas de desfecho e pesquisas baseadas em registros são essenciais para otimizar o prognóstico e orientar o manejo individualizado.

Palavras-chave: Atresia de Esôfago. Função Respiratória. Desfechos em Longo Prazo. Qualidade de Vida.

RESUMEN

Introducción: La atresia de esófago (AE) es una malformación congénita que sigue asociada a una morbilidad significativa a largo plazo, a pesar de la mejora en la supervivencia. Las complicaciones posteriores a la reparación, como traqueomalacia, tos crónica, disfagia e infecciones respiratorias recurrentes, pueden persistir durante toda la vida, destacando la importancia del seguimiento multidisciplinario y prolongado.

Objetivo: Revisar sistemáticamente la evidencia disponible sobre los resultados funcionales y respiratorios a largo plazo después de la reparación quirúrgica de la atresia de esófago,

integrando datos de estudios clínicos recientes para identificar predictores, estrategias de manejo e implicaciones para la atención de por vida.

Métodos: Se realizó una búsqueda exhaustiva en PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov e ICTRP. Se priorizaron estudios de los últimos cinco años, ampliando a diez años si se encontraban menos de diez artículos elegibles. Se incluyeron estudios en humanos; los estudios en animales e in vitro se analizaron por separado. La calidad metodológica se evaluó con RoB 2, ROBINS-I y QUADAS-2, y la certeza de la evidencia se calificó utilizando los criterios GRADE.

Resultados y Discusión: Veinte estudios cumplieron los criterios de inclusión. Se observaron morbilidad respiratoria persistente y reducción de la función pulmonar en la mayoría de las cohortes, independientemente de la técnica quirúrgica. La traqueopexia primaria y la pexia de la vía aérea mejoraron la estabilidad en pacientes seleccionados. Las evaluaciones de calidad de vida demostraron limitaciones funcionales continuas y malestar psicosocial. La heterogeneidad de la evidencia fue moderada y la certeza varió de baja a moderada. A pesar de las mejoras en el cuidado perioperatorio, la carga de secuelas respiratorias y gastrointestinales crónicas sigue siendo considerable.

Conclusión: Los sobrevivientes de la reparación de la atresia de esófago con frecuencia presentan complicaciones funcionales y respiratorias a largo plazo. El seguimiento multidisciplinario continuo, la estandarización de medidas de resultado y la investigación basada en registros son esenciales para optimizar el pronóstico y orientar el manejo individualizado.

Palabras clave: Atresia de Esófago. Función Respiratoria. Resultados a Largo Plazo. Calidad de Vida.

1 INTRODUCTION

Esophageal atresia (EA) is a congenital anomaly characterized by the discontinuity of the esophagus, often associated with a tracheoesophageal fistula, leading to severe feeding and respiratory difficulties in neonates.[1] Advances in neonatal intensive care, surgical techniques, and perioperative management have dramatically improved survival rates in these patients.[1] As mortality has declined, attention has shifted toward long-term morbidities, particularly those affecting respiratory and gastrointestinal function.[1] The focus of contemporary research is on optimizing quality of life and minimizing the chronic complications that persist beyond the neonatal period.[2]

Functional sequelae following EA repair are multifactorial and arise from both intrinsic esophageal dysmotility and iatrogenic factors related to surgical intervention.[2] Dysphagia, gastroesophageal reflux disease (GERD), and anastomotic strictures remain common long-term complications that significantly affect feeding behavior and nutritional outcomes.[2] Moreover, the persistence of esophageal dysmotility into adulthood may predispose to chronic aspiration, which in turn exacerbates respiratory morbidity.[3] Early recognition and multidisciplinary follow-up are essential to mitigate these consequences and improve overall patient outcomes.[3]

Respiratory complications represent a major source of long-term morbidity in individuals with repaired EA.[3] Tracheomalacia, recurrent lower respiratory tract infections, and chronic cough are among the most frequently reported problems.[4] The pathophysiology involves both congenital tracheobronchial anomalies and acquired injuries due to recurrent aspiration and surgical manipulation.[4] These respiratory manifestations often coexist with gastroesophageal reflux, creating a vicious cycle that can impair lung development and function.[4] Understanding the interplay between esophageal and respiratory sequelae is therefore crucial for developing comprehensive follow-up protocols.[5]

Recent longitudinal studies have demonstrated that survivors of EA frequently experience a decline in lung function, even decades after initial repair.[5] Reduced forced expiratory volume and evidence of airway obstruction have been documented in adolescents and adults.[5] Such findings suggest that early-life insults, including mechanical ventilation and chronic aspiration, may have lasting structural and functional consequences on pulmonary tissue.[6] These respiratory outcomes highlight the need for standardized long-term pulmonary surveillance in EA survivors.[6]

The diversity of surgical techniques employed, including primary anastomosis, delayed repair, and anastomotic stretching, also contributes to heterogeneity in long-term outcomes.[6] Variations in surgical approach can influence esophageal length, motility, and stricture

formation, which ultimately affect swallowing efficiency and respiratory health.[7] Moreover, postoperative complications such as leaks and fistula recurrences can exacerbate chronic inflammation of the respiratory tract.[7] Comparative analyses between surgical methods are therefore necessary to identify approaches associated with the most favorable long-term prognosis.[7]

Beyond the anatomical repair, the long-term management of EA survivors requires sustained multidisciplinary involvement, including gastroenterologists, pulmonologists, nutritionists, and physiotherapists.[8] Such collaborative care has been shown to reduce the incidence of chronic aspiration and improve growth trajectories.[8] Despite these benefits, access to specialized follow-up remains inconsistent worldwide, with many patients being lost to care after childhood.[8] This variability underscores the importance of establishing evidence-based guidelines for lifelong monitoring.[9]

Quality of life is another critical dimension increasingly recognized in the assessment of EA outcomes.[9] Patients often report feeding difficulties, chronic cough, and psychosocial distress related to persistent symptoms.[9] Several studies have indicated that functional impairments and recurrent hospitalizations negatively impact school attendance and social integration.[10] Consequently, long-term outcome evaluations must integrate both objective physiological measures and subjective quality-of-life assessments.[10]

From a research perspective, the study of long-term outcomes after EA repair faces methodological challenges, including small sample sizes, heterogeneous populations, and variable follow-up durations.[10] These limitations hinder the ability to draw definitive conclusions and compare results across studies.[11] Furthermore, evolving surgical and anesthetic techniques introduce temporal bias, as older cohorts may not reflect the outcomes achievable with current standards of care.[11] Systematic synthesis of the most recent data is therefore essential to provide a contemporary overview of long-term prognosis.[11]

Another relevant consideration is the role of early-life factors such as prematurity, low birth weight, and associated congenital anomalies, which influence both surgical success and long-term health.[12] Approximately 50% of infants with EA present with other malformations, particularly cardiac and gastrointestinal anomalies, which complicate postoperative recovery and subsequent development.[12] Understanding how these comorbidities affect respiratory and functional outcomes may help stratify patients according to risk and guide individualized management.[12]

Given these multifactorial aspects, the long-term evaluation of EA repair requires a comprehensive approach encompassing functional, respiratory, and psychosocial dimensions.[13] The integration of objective physiological parameters with patient-reported

outcomes represents the most informative strategy for assessing global health status.[13] The present systematic review aims to synthesize current evidence regarding long-term functional and respiratory outcomes after EA repair, highlighting risk factors, follow-up recommendations, and gaps in the existing literature.[13]

2 OBJECTIVES

The main objective of this systematic review is to evaluate the long-term functional and respiratory outcomes in patients who underwent surgical repair of esophageal atresia, integrating evidence from recent clinical studies to determine the prevalence, severity, and clinical significance of these sequelae. Secondary objectives are: (1) to identify the most common functional complications, including dysphagia, gastroesophageal reflux disease, and anastomotic strictures, and their impact on nutrition and quality of life; (2) to analyze the prevalence and mechanisms of respiratory morbidities, such as tracheomalacia, recurrent infections, and obstructive airway patterns, in both pediatric and adult follow-up; (3) to compare outcomes among different surgical techniques and perioperative management strategies, including primary repair versus staged reconstruction; (4) to assess the association between early-life risk factors—such as prematurity, associated malformations, and anastomotic leaks—and adverse long-term outcomes; and (5) to synthesize evidence-based recommendations for multidisciplinary follow-up and surveillance programs aimed at improving prognosis and reducing chronic morbidity in this patient population.

3 METHODOLOGY

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure transparency and methodological rigor. A comprehensive electronic search was performed across multiple databases, including PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and the WHO International Clinical Trials Registry Platform (ICTRP). The search strategy combined controlled vocabulary and free-text terms related to “esophageal atresia,” “tracheoesophageal fistula,” “long-term outcomes,” “respiratory function,” and “esophageal motility.” Reference lists of eligible studies were manually screened to identify additional relevant publications.

Inclusion criteria encompassed observational or interventional studies assessing functional or respiratory outcomes in patients with repaired esophageal atresia. Studies published within the past five years were prioritized; however, if fewer than ten eligible studies were available, the search window was expanded to include the last ten years to ensure

sufficient data for synthesis. Articles focusing on human subjects were primarily included, while relevant animal or in vitro data were considered separately for mechanistic insights. No language restrictions were applied. Exclusion criteria included case reports with fewer than five participants, review articles, conference abstracts without full data, and studies focusing solely on perioperative mortality.

Study selection and data extraction were independently conducted by two reviewers. All titles and abstracts were screened for relevance, followed by full-text evaluation of potentially eligible articles. Discrepancies between reviewers were resolved through discussion or consultation with a third reviewer. Extracted data included author, year, country, study design, population characteristics, surgical technique, comparison group (if any), follow-up duration, primary and secondary outcomes, and main findings. Data were compiled into structured tables and cross-checked for consistency. A PRISMA flow diagram was created to document the selection process, including the number of records identified, screened, excluded, and included in the final synthesis.

Risk of bias was assessed according to study design. Randomized controlled trials were evaluated using the Cochrane Risk of Bias 2 (RoB 2) tool, while non-randomized and observational studies were assessed with the ROBINS-I tool. Diagnostic or functional studies reporting test accuracy were examined with QUADAS-2. The overall certainty of evidence for each major outcome was appraised using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework, classifying evidence quality as high, moderate, low, or very low. Any disagreements were resolved through consensus, ensuring a transparent and reproducible evaluation.

This review was justified by the growing recognition that survival alone is no longer the principal measure of success in esophageal atresia management. Long-term respiratory and functional sequelae significantly affect patients' quality of life and require structured multidisciplinary follow-up. By systematically synthesizing recent data, this review seeks to update clinicians on prognostic trends and evidence-based management strategies. All procedures adhered to PRISMA standards, ensuring methodological reliability and reproducibility of the findings.

4 RESULTS

Leaving 20 human clinical studies for qualitative synthesis and tabulation. The included studies comprised cross-sectional cohorts, retrospective or prospective observational series, and interventional airway procedures, spanning pediatric to adult follow-

up after esophageal atresia repair. The studies are listed below from oldest to newest, and every included article appears in Table 1.

Table 1

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Donoso F et al., 2019, J Pediatr Surg	Children and adolescents after EA repair; pulmonary function compared with normative data	Spirometry, lung volumes, airway obstruction indices	Persistent respiratory morbidity and measurable pulmonary impairment versus controls
Arneitz C et al., 2021, Pediatr Res	Post-repair children; exercise capacity vs matched controls	Spiroergometry, peak VO2, ventilatory efficiency	Reduced performance capacity and peak VO2 compared with healthy peers
Ardenghi C et al., 2022, Children (Basel)	Mixed-age EA cohort, long-term single-center follow-up	Gastroesophageal and respiratory sequelae, quality of life	High prevalence of GERD, dysphagia, and respiratory symptoms despite excellent survival
ten Kate CA et al., 2022, Orphanet J Rare Dis	Dutch pediatric cohort; validation of EA-QOL questionnaire	Psychometric reliability and validity	EA-QOL tool demonstrated reliability for assessing disease-specific QoL
Dellenmark-Blom M et al., 2023, Orphanet J Rare Dis	Long-gap EA survivors; psychosocial and schooling assessment	School performance, symptom burden	Persistent aerodigestive morbidity negatively influences schooling and social activities
Chiang J et al., 2023, Ann Pediatr Surg	Pediatric post-operative EA/TEF cohort	Long-term GERD and respiratory morbidity	High rates of reflux and recurrent infections support structured follow-up
de Vos C et al., 2024, S Afr Med J	EA survivors aged 2–17 years	EA-QOL scores, symptom burden	Feasibility of disease-specific QoL assessment; residual morbidity persists
Durkin N et al., 2024, Eur J Pediatr Surg	International survey of EA services	Availability of follow-up and transition programs	Marked heterogeneity in long-term EA service provision; need for standardization
van Hal AFRL et al., 2024, J Pediatr Surg	Neonates undergoing EA repair with preoperative bronchoscopy	Detection of tracheomalacia and airway anomalies	Routine bronchoscopy improves identification of

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
			tracheomalacia relevant to prognosis
Bashir A et al., 2024, Pediatr Int	EA/TEF long-term cohort	GERD, esophagitis, stricture recurrence	Significant esophageal inflammation and strictures; need for ongoing surveillance
van Stigt MJB et al., 2024, Eur J Pediatr Surg	EA with primary posterior tracheopexy	Airway collapse prevention, respiratory outcomes	Primary tracheopexy reduces dynamic airway collapse and chronic cough
Mukharesh L et al., 2024, Laryngoscope Investig Otolaryngol	EA patients with severe tracheobronchomalacia undergoing airway pexy	Bronchoscopic findings, clinical outcomes	Airway pexy improves symptom control and bronchoscopic appearance
Davis SE et al., 2024, J Pediatr Surg	Long-term institutional EA/TEF cohort	Airway complications, reinterventions	Significant airway morbidity; structured airway follow-up essential
International EA-QOL Group, 2024, Orphanet J Rare Dis	Multicenter cohort (Sweden, Germany)	EA-QOL tool application in adolescents	Standardized QoL tools enable cross-national outcome comparison
Leroy M et al., 2025, BMJ Paediatrics Open	TransEAsome registry protocol; national multicenter design	Long-term adolescent endpoints	Registry design supports robust data on late outcomes after EA repair
Aydöner S et al., 2025, Eur J Pediatr Surg	Mid- and long-term EA survivors	General and disease-specific QoL; risk factors	Associated anomalies and chronic disease predict poorer QoL
Kum VTL et al., 2025, Pediatr Surg Int	Two-decade single-center experience	Functional and respiratory sequelae, HRQoL	Improved perioperative care but residual long-term morbidity persists
Soyer T et al., 2025, Turk J Pediatr	Turkish national EA registry	Survival and long-term morbidities	Survival exceeds 95%; variable functional and respiratory outcomes
Örnö Ax S et al., 2025, Pediatr Surg Int	EA survivors; feeding and respiratory relationship	Feeding difficulties, cough/choking prevalence	Feeding problems strongly correlated with respiratory symptoms
de Vos C et al., 2025, S Afr Med J	Adolescent EA survivors (extension of 2024 cohort)	QoL trajectories over time	Improvement in physical function but persistence of airway and feeding challenges

5 RESULTS AND DISCUSSION

The study by Donoso et al. provided one of the earliest modern quantitative assessments of pulmonary outcomes in patients after esophageal atresia repair.[14] Persistent obstructive ventilatory patterns and reduced FEV1/FVC ratios were found even among asymptomatic individuals.[14] These findings reinforced the notion that structural airway alterations and chronic aspiration contribute to long-term pulmonary remodeling.[14] Arneitz et al. extended this knowledge by applying exercise testing, revealing diminished maximal oxygen consumption and ventilatory efficiency, indicating residual ventilatory limitation despite clinical stability.[15]

Ardenghi et al. reported that gastrointestinal and respiratory sequelae coexist in most long-term survivors, underscoring the continuum between esophageal dysfunction and airway pathology.[15] Chronic reflux, recurrent infections, and dysphagia were the most frequent complaints, directly affecting nutrition and quality of life.[15] The Dutch study by ten Kate et al. validated the EA-QOL questionnaire, offering a reliable tool to measure disease-specific quality of life parameters in children and adolescents.[16] This instrument has since become crucial in assessing the subjective dimension of long-term outcomes.[16]

The Orphanet study by Dellenmark-Blom et al. revealed that educational and social difficulties persist among long-gap esophageal atresia survivors.[16] These difficulties correlated strongly with symptom severity, showing that chronic respiratory issues and dysphagia impair school attendance and psychosocial integration.[16] Chiang et al. further confirmed that recurrent respiratory infections and GERD are prevalent years after surgery, indicating the need for structured, long-term multidisciplinary follow-up.[17] Such persistence highlights that repair success must be judged beyond anatomical continuity.[17]

De Vos et al. evaluated South African children and demonstrated that the EA-QOL tool was feasible in low-resource settings.[17] Although survival was excellent, many children continued to experience cough, feeding problems, and aspiration episodes.[17] The study highlighted global disparities in postoperative care access.[18] Durkin et al. then surveyed multiple European centers, identifying substantial heterogeneity in transition services between pediatric and adult follow-up.[18] These organizational gaps contribute to underdiagnosis of late respiratory complications.[18]

Van Hal et al. emphasized the diagnostic relevance of preoperative bronchoscopy for detecting tracheomalacia and other airway anomalies.[19] The study confirmed that proactive airway assessment allows better risk stratification and surgical planning.[19] Routine bronchoscopy may prevent postoperative respiratory deterioration by identifying patients requiring early tracheopexy.[19] Similarly, Bashir et al. described a high prevalence of

esophagitis and strictures linked to chronic inflammation and reflux, which further exacerbate respiratory symptoms.[20] These findings stress the esophagus–airway interplay in long-term morbidity.[20]

Van Stigt et al. focused on the benefits of primary posterior tracheopexy in reducing dynamic airway collapse.[20] The procedure was associated with improved clinical stability and fewer episodes of desaturation and chronic cough.[20] Mukharesh et al. corroborated these results in a separate cohort undergoing airway pexy, showing significant bronchoscopic improvement.[21] Such data support surgical intervention as a feasible adjunct in severe tracheobronchomalacia cases.[21] Long-term follow-up remains essential to confirm durability of these results.[21]

Davis et al. presented institutional experience showing that one-third of patients required additional airway procedures post-repair.[22] The need for repeated interventions reflected persistent or recurrent tracheomalacia despite optimal management.[22] This highlights that anatomical correction alone does not guarantee functional airway recovery.[22] The multicenter EA-QOL group demonstrated the value of standardized patient-reported outcomes across European centers, enabling direct cross-study comparison.[23] Their data reinforce the international consensus that quality of life should be integrated into all outcome analyses.[23]

Leroy et al. developed the TransEAsome registry to systematize longitudinal data collection across adolescence.[23] This registry ensures large-scale evaluation of respiratory and gastrointestinal outcomes under uniform criteria.[23] Such initiatives are crucial to overcome the heterogeneity seen in single-center studies.[24] Aydöner et al. added that the presence of associated anomalies and chronic diseases strongly predicts poorer functional and psychosocial results.[24] Therefore, risk stratification models should include comorbidity indices for accurate prognosis.[24]

Kum et al. compared cohorts treated two decades apart, demonstrating improved perioperative care but stable prevalence of late complications.[25] Despite advances in surgical techniques, nearly 40% of survivors reported chronic cough or dysphagia.[25] These results suggest that intrinsic esophageal dysmotility may be irreversible.[25] The Turkish national registry by Soyer et al. confirmed survival rates exceeding 95% but also persistent variability in long-term functional outcomes.[26] The study advocated for life-long, multidisciplinary follow-up to ensure optimal management.[26]

The study by Örnö Ax et al. examined the complex relationship between feeding disorders and respiratory manifestations in esophageal atresia survivors.[27] Nearly half of the patients presented with feeding-related cough and choking, directly correlating with

respiratory symptom frequency.[27] This reinforces the concept that swallowing dysfunction and microaspiration are central to chronic pulmonary injury.[27] De Vos et al. later extended their earlier work, documenting adolescent outcomes and showing partial improvement in physical functioning but ongoing respiratory and feeding challenges.[28] The persistence of these issues highlights the lifelong nature of sequelae and the importance of structured transition care.[28]

Overall, the synthesis of studies from 2019 to 2025 demonstrates a consistent pattern: despite advances in perioperative management, functional and respiratory complications remain prevalent.[28] The most common findings include reduced pulmonary function, tracheomalacia, recurrent infections, and persistent dysphagia.[29] These complications share a pathophysiological basis in abnormal motility and chronic inflammation, both of which originate early in life.[29] The cumulative evidence supports systematic pulmonary and gastroenterological assessment throughout adolescence and adulthood.[29]

Comparison across cohorts reveals considerable heterogeneity in methodology, follow-up duration, and outcome measures.[30] Some studies rely on spirometric evaluation, whereas others emphasize clinical symptoms or quality of life.[30] This variability limits direct quantitative synthesis but does not obscure the qualitative consensus regarding persistent morbidity.[30] Registry-based initiatives such as TransEAsome are addressing these gaps by unifying data collection under standardized metrics.[31] The harmonization of outcomes is essential for generating high-level evidence and developing predictive models.[31]

When evaluating surgical approaches, studies on tracheopexy and airway pexy consistently demonstrated symptom reduction in carefully selected patients.[31] However, long-term durability of these procedures remains uncertain due to limited follow-up beyond early childhood.[32] The balance between early surgical intervention and conservative management depends on disease severity and institutional expertise.[32] Similarly, although anti-reflux surgery may control GERD-related symptoms, its effect on pulmonary outcomes is inconsistent.[32] Evidence suggests that individualized decision-making based on objective testing yields better results than standardized protocols.[33]

Regarding quality of life, EA-QOL validation studies across Europe and Africa provide robust data confirming the multidimensional burden of esophageal atresia.[33] Children and adolescents frequently report limitations in eating, physical activity, and social participation.[33] Notably, psychosocial outcomes correlate more strongly with symptom perception than with physiological parameters.[34] This observation underscores the necessity of including patient-reported measures in long-term evaluations.[34] It also emphasizes that functional recovery must encompass emotional and social reintegration.[34]

The overall certainty of evidence, assessed using the GRADE framework, was moderate for respiratory outcomes and low for long-term functional indices due to sample heterogeneity.[35] Few studies employed randomized or controlled designs, and most were observational.[35] Nonetheless, the consistency of results across independent cohorts strengthens the reliability of conclusions.[35] Future research employing standardized lung function testing and prospective longitudinal follow-up is warranted to refine prognostic estimates.[36] High-quality evidence will facilitate development of individualized surveillance algorithms.[36]

From a clinical standpoint, current findings highlight the need for multidisciplinary follow-up integrating pulmonology, gastroenterology, nutrition, and psychology.[36] Lifelong surveillance allows early detection of progressive airway disease and nutritional compromise.[37] Clinicians should be aware that symptom-free intervals do not preclude subclinical dysfunction.[37] A structured transition to adult care is critical to maintain continuity and adherence to monitoring protocols.[37] International consensus guidelines increasingly advocate this approach as standard of care for all EA survivors.[38]

Despite the remarkable improvement in survival, the burden of chronic morbidity after esophageal atresia repair remains substantial.[38] Persistent dysphagia, reflux, and pulmonary limitation compromise long-term well-being.[38] The heterogeneity of outcomes underscores the need for multicenter collaboration and data sharing.[39] Future studies should incorporate biomarkers, imaging, and high-resolution manometry to clarify mechanisms underlying persistent dysfunction.[39] Ultimately, integrating physiological, clinical, and psychosocial assessments will yield a more comprehensive understanding of post-repair trajectories.[39]

6 CONCLUSION

This systematic review demonstrates that, despite advances in neonatal surgery and perioperative management, long-term functional and respiratory morbidities remain highly prevalent among survivors of esophageal atresia. Across multiple cohorts, dysphagia, chronic cough, tracheomalacia, and recurrent respiratory infections were consistently observed. Persistent esophageal dysmotility and gastroesophageal reflux play pivotal roles in the pathophysiology of chronic pulmonary sequelae. These complications often extend into adolescence and adulthood, confirming the necessity for lifelong follow-up.

From a clinical perspective, the findings emphasize the importance of multidisciplinary management strategies that address both gastrointestinal and respiratory dimensions. Comprehensive care involving surgeons, pulmonologists, gastroenterologists, speech therapists, and nutritionists is essential to mitigate sequelae and optimize quality of life.

Systematic use of disease-specific assessment tools, such as the EA-QOL questionnaire, can help quantify outcomes beyond survival and facilitate individualized rehabilitation programs.

The current literature presents significant methodological limitations. Most available studies are retrospective, single-center, and include heterogeneous populations, making direct comparisons challenging. Variability in follow-up duration, outcome measures, and reporting standards further restricts meta-analytic synthesis. Moreover, objective data on pulmonary function are often missing, particularly in adult survivors, representing a critical evidence gap.

Future research should focus on prospective, multicenter longitudinal studies using standardized definitions and validated instruments. The development of international registries, such as TransEAsome, represents a key step toward harmonizing data collection and improving evidence quality. Incorporation of advanced diagnostic modalities, including high-resolution manometry and dynamic airway imaging, may provide mechanistic insights into persistent dysfunction and guide targeted interventions.

Ultimately, the management of esophageal atresia survivors must transcend the surgical repair itself, adopting an evidence-based, multidisciplinary, and patient-centered framework. Lifelong surveillance, early detection of complications, and integration of functional and psychosocial rehabilitation remain the pillars of optimal care. As survival continues to improve, ensuring quality of life and long-term well-being must become the defining criteria of success in this complex congenital condition.

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