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Effects of Postoperative Complications on Overall Survival Following Esophagectomy: A Meta-Analysis Using the Restricted Mean Survival Time Analysis

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ABSTRACT

Objective: This study aims to conduct a comprehensive meta-analysis of the effects of postoperative complications (PCs) on survival following esophagectomy using the restricted mean survival time (RMST) analysis.

Methods: A systematic literature search was performed in PubMed, Embase, Web of Science, Cochrane, and Medline, including articles published up to July 2024. Data were reconstructed from Kaplan–Meier curves, and the difference in RMST (RMSTD) and the RMST/restricted mean time loss (RMTL) ratios were calculated to examine the effects of PCs on overall survival.

Results: A total of 12 articles, including 7925 patients, met the inclusion criteria. RMSTD estimates indicate that patients with overall PCs survived an average of 0.04 years shorter (RMSTD = -0.04, 95% CI: −0.06, −0.03) than those without PCs at the 1-year follow-up and 0.39 years shorter (RMSTD = −0.39, 95% CI: −0.55, −0.22) at the 5-year follow-up. Patients with anastomotic leaks survived an average of 0.34 years shorter (RMSTD = −0.34, 95% CI: −0.49, −0.19), and patients with pulmonary complications survived an average of 0.63 years shorter (RMSTD = −0.63, 95% CI: −0.81, −0.45) at the 5-year follow-up. Additionally, RMTL ratios were estimated to be 1.21 (95% CI: 1.12, 1.31) for overall PCs, 1.19 (95% CI: 1.11, 1.28) for anastomotic leaks, and 1.53 (95% CI: 1.36, 1.73) for pulmonary complications at the 5-year follow-up, respectively.

Conclusions: Our findings quantified the annual negative impact of PCs of esophageal cancer on overall patient survival following esophagectomy. Increased efforts are needed to enhance prevention, early screening, and timely treatment for complications, particularly for patients with pulmonary complications.

1 | Introduction

Esophageal cancer is often associated with a poor prognosis and a high mortality rate, as a considerable cause of cancer deaths and a substantial healthcare burden globally [1]. According to the Global Burden of Disease Study 2017, there were approximately 473000 new cases and 436000 deaths of esophageal cancer [2]. Surgical treatment is widely used for patients with various stages and types of esophageal cancer to improve survival rates [3]. However, despite significant advancements in surgical techniques, perioperative management, and neoadjuvant therapy, surgical resection combined with lymphadenectomy remains the primary treatment for localized esophageal cancer in recent years, postoperative complications (PCs) following esophagectomy remain a critical issue that needs to be addressed [4, 5]. Even in certain high-volume medical centers, the incidence of severe PCs remains as high as 20%, which is associated with increased hospital stays, medical costs, and mortality rates within 90 days [6]. The Esophagectomy Complications Consensus Group (ECCG) established consensus definitions for complications after esophagectomy in 2015 [7]. Prior studies identified that common PCs include anastomotic leaks and pneumonia, which severely impact patients' overall survival rates and other survival metrics [8]. Moreover, although extensive research exists on surgical techniques and perioperative management, studies addressing PCs and their impact on survival are relatively insufficient, particularly regarding the application of newer methods.

In recent years, the difference in restricted mean survival time (RMSTD) has increasingly been used either in conjunction with or as a substitute for the hazard ratio (HR) in meta-analyses [9]. Restricted mean survival time (RMST) is the average survival time up to a predetermined time and graphically corresponds to the area under the survival curve [10]. The RMSTD can be expressed as the number of life years gained from one arm compared to the other. RMSTD may have several advantages over HR. First, RMSTD stays valid even when the proportional hazards assumption is not met unlike HR. Second, RMSTD is an absolute outcome that depends on both baseline risk and relative treatment effect, whereas HR reflects only the relative treatment effect [10]. Third, interpreting treatment differences on a time scale is generally considered easier, particularly from a clinical perspective. For example, one study empirically compared RMSTD with HR across 54 randomized controlled trials and found that HR may appear large when absolute effects are small and RMST-based measurements should be routinely reported in randomized trials with time-to-event outcomes [11]. The concept of RMST was first introduced by Dr. Irwin in 1949 and has gained attention since around 2013 as an alternative to address the limitations of traditional methods [10, 12]. Over the past decade, RMST has been recommended as an alternative measure of treatment effect in methodological guidelines published by Health Technology Assessment (HTA) agencies in countries such as the United Kingdom, Canada, and Australia [13]. The UK's National Institute for Health and Care Excellence (NICE) widely uses RMST as a measure of treatment effect and as a tool to validate estimates of extrapolated mean survival in cost-utility analyses [14].

Therefore, this study aims to conduct a comprehensive meta-analysis of the effects of PCs on survival by calculating RMSTDs to update the evidence regarding PCs following esophagectomy.

2 | Methods

2.1 | Information Sources and Search Strategy

This meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guideline [15] and was registered with PROSPERO (www.crd.york.ac.uk/PROSPERO, registration number: CRD42024569782).

A systematic literature search was performed in PubMed, Embase, Web of Science, Cochrane, and Medline, covering articles up to July 2024. The search used a combination of the following MeSH (Medical Subject Headings) terms: ("esophageal cancer", "esophageal neoplasm", "esophageal tumor") AND ("postoperative compl*", "complication") AND ("survival", and "overall surv*"). The complete search strategy is detailed in Supplementary Table S1.

2.2 | Eligibility Criteria

Studies were included based on the following criteria: (1) the study design was either a retrospective or prospective cohort study; (2) the study sample included patients diagnosed with esophageal cancer who underwent an esophageal cancer surgery; (3) the types of complications were defined according to the 2015 ECCG guideline; (4) the reported outcomes included the overall survival rate; (5) the study presented Kaplan–Meier curves to compare the survival impact of complications in the context of esophageal cancer surgeries. We excluded letters, commentaries, case reports, conference abstracts, reviews, unpublished articles, and non-English publications due to insufficient information for assessment and analysis.

2.3 | Study Selection and Data Extraction

First, all articles were imported into the EndNote X9 database, and one author (C.Y.H.) removed duplicate entries both automatically and manually. Second, three authors (C.Y.H., Z.Q., and L.L.) independently screened the titles and abstracts and reviewed the full texts based on the established eligibility criteria. Third, another two authors (Y.B.Y. and H.Z.) addressed any discrepancy in the results to resolve the disagreements. Finally, two authors (C.Y.H. and L.L.) extracted the following variables: the first author, publication time, study country, study design, demographics (i.e., sample size, age, and sex), tumor characteristics (histology and location), and details of surgical treatment (i.e., surgical method and pathological tumor staging). Kaplan–Meier curves for survival variables were also collected.

2.4 | Outcomes

The outcome is overall survival (OS), defined as the time interval between surgery and follow-up or any cause-of-death. The OS data were obtained from Kaplan–Meier curves presented in selected articles.

According to the ECCG, overall PCs included anastomotic leaks, conduit necrosis or failure, recurrent laryngeal nerve injury, chyle leak severity, gastrointestinal complications, pulmonary complications, cardiac complications, thromboembolic complications, urologic complications, infections, neurologic or psychiatric complications, wound or diaphragm. We focused on overall PCs, anastomotic leaks and pulmonary PCs. The subgroup of anastomotic leaks and pulmonary PCs were specified because they were the most prevalent complications after esophagectomy, as well as the number of selected articles could support the analyses.

2.5 | Quality Assessment

Risk of Bias in Non-Randomized Studies of Interventions (ROBINS-I) was used to assess the risk of various biases, including confounding, selection, classification, intervention, missing data, and outcome measurement [16]. Three authors (C.Y.H., X.X., and Y.B.Y.) classified each study into one of four categories: low, moderate, serious, and critical risk of bias (Supplementary Table S2).

2.6 | Kaplan–Meier Reconstruction and Data Analysis

Following the method used by Guyot [17], we digitized the Kaplan–Meier curves using the Get Data Graph Digitizer software and reconstructed individual patient time-to-event data with the Enhanced Kaplan–Meier Curves software. This approach helps mitigate potential biases in aggregated data, thereby improving the accuracy of the results [10].

We calculated RMSTDs, the RMST ratios and the restricted mean time loss ratios (RMTL ratios) across time-points using the 'survRM2' package, while controlling for sample size-based weights as covariates. RMSTD is an absolute measure of survival time lost for patients with PCs following esophagectomy compared to those without PCs, RMST ratio refers to the ratio of a patient's actual survival time at a given time point (e.g., 1-year) relative to the baseline survival time, and RMTL ratio represents the ratio of survival time lost due to pulmonary complications or other factors, relative to baseline survival time. To account for variability in follow-up durations across studies, we computed RMSTDs, RMST, and RMTL ratios at time cut-off points using 1-year incremental intervals (0–1 year, 0–2 years, 0–3 years, 0–4 years, and 0–5 years). Statistical significance was defined as a two-sided p-value of less than 0.05. All analyses were performed using R software (version 4.3.2, R Foundation, Vienna, Austria).

3 | Results

3.1 | Study Characteristics

The initial search yielded a total of 23 769 relevant articles from the following databases (Figure 1): PubMed ($n = 2403$), Embase ($n = 5453$), Web of Science ($n = 10\,595$), Cochrane ($n = 521$), and Medline ($n = 4797$). After removing duplicate records, we reviewed 13 302 titles and abstracts to select 40 articles for full-text review. Ultimately, there were 12 articles, including 7925 patients receiving esophagectomy, identified as meeting the inclusion and exclusion criteria for the subsequent RMSTD analysis (Table 1). Of 7381 patients, ages ranged from 21 to 88 years, and 80% were male. Of 6774 patients reported specific cancer types in nine articles, about 60% were esophageal adenocarcinoma, about 38% were esophageal squamous cell carcinoma, and about 2% were other types. Of 6522 patients reported tumor pathology staging based on American Joint Committee on Cancer (AJCC) 6th, 7th, and 8th editions in 8 articles, Stage 0 to I accounts for 36%, Stage II accounts for 24%, Stage III accounts for 36%, and Stage IV accounts for 4%. We also described minimally invasive, hybrid, and open Ivor Lewis or McKeown esophagectomies, but there were differences in anastomosis techniques in the included studies, primarily depending on surgeon's preference.

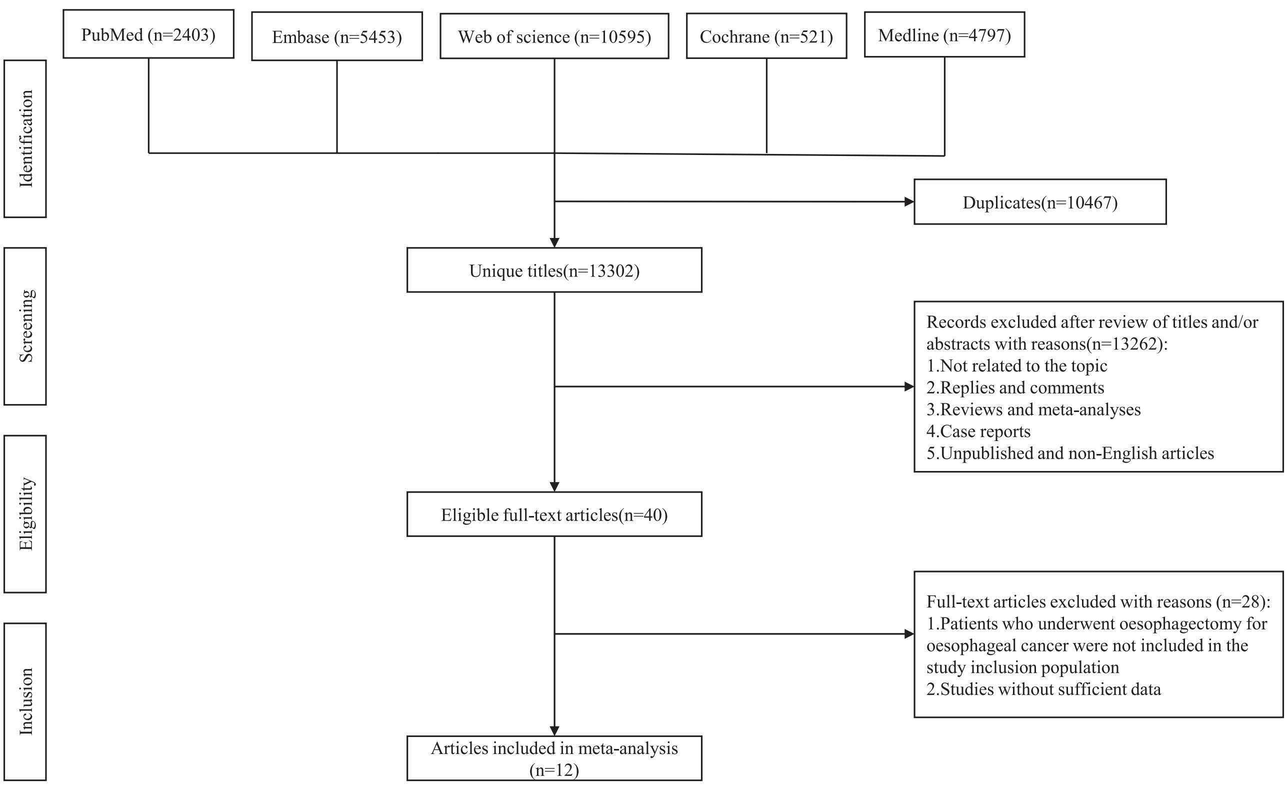

FIGURE 1 | Flowchart of the systematic search and selection process.

TABLE 1 | Study characteristics of included studies.

Author (year)	Country	Study design	Number of patients	Age (year)	Sex, Male %	Tumor histology[a]	Location[b]	Stage 0–I[c]	Stage II[c]	Stage III[c]	Stage IV[c]	Surgical method
Fransen et al. (2021) [18]	Multicenter	PCS	915	63 ± 8.8	739	193–722	Proximal 42, Distal 873	452	216	238	9	MIE
Junemann-Ramirez et al. (2005) [19]	UK	RCS	276	66 (9.2)	188	NA	NA	12	70	185	9	Hyb
Booka et al. (2015) [20]	Japan	RCS	284	NA	256	255–19–10	40–140–104	86	73	112	13	Hyb
Kamarajah et al. (2020) [21]	UK	PCS	1063	65 (58–71)	811	207–856	NA	292	234	450	87	Open/Hyb/MIE
Markar et al. (2015) [22]	Multicenter (EUR)	RCS	2439	60 (21–88)	2000	1105–1260–74	281–828–1330	1043	570	826	0	Open/Hyb
Martin et al. (2005) [23]	USA	RCS	476	60 (23–84)	381	60–399–17	0–42–434	132	157	144	42	Open
Rutegard et al. (2012) [24]	Sweden	PCS	567	NA	460	135–432	NA	110	166	230	58	Open/Hyb
Van Daele et al. (2016) [25]	Belgium	RCS	412	62 (11)	318	107–248	NA	NA	NA	NA	NA	Open/Hyb
Aahlin et al. (2016) [26]	Norway	RCS	331	NA	257	NA	NA	NA	NA	NA	NA	Open/Hyb/MIE
Baba et al. (2016) [27]	Japan	RCS	502	65.7 ± 9	445	502–0–0	NA	225	85	156	36	Open/Hyb/MIE
Luc et al. (2015) [28]	France	RCS	116	64.6 (40–79)	106	0–106–0	0–0–116	NA	NA	NA	NA	Open
Yoshida et al. (2022) [29]	Japan	PCS	544	NA	NA	NA	NA	NA	NA	NA	NA	Open/MIE

Abbreviations: Hyb: hybrid esophagectomy; MIE: minimally invasive esophagectomy; NA: not available; PCS: prospective cohort study; RCS: retrospective cohort study.
[a]Squamous cell carcinoma-adenocarcinoma-other.
[b]Upper–medium–lower esophagus.
[c]American Joint Committee on Cancer 6th, 7th, and 8th editions.

3.2 | Estimated RMSTD in OS for Patients With Overall PCs

Five articles reported data on patients with overall PCs [18, 24, 26–28]. The estimated RMSTD in OS indicated that patients with overall PCs consistently demonstrated a lower RMST compared to those without PCs (Figure 2A, Table 2). At the 1-year follow-up, the estimated RMSTD was −0.04 years (95% CI: −0.06, −0.03), suggesting that patients with overall PCs lived an average of 0.04 years shorter than those without PCs. At the 2-year follow-up, patients with overall PC lived an average of 0.14 years less (RMSTD = −0.14, 95% CI: −0.19, −0.09). At the 5-year follow-up, patients with overall PCs lived an average of 0.39 years less (RMSTD = −0.39, 95% CI: −0.55, −0.22), and the RMST ratio was estimated to be 0.88 (95% CI: 0.83–0.93) while the RMTL Ratio was estimated to be 1.21 (95% CI: 1.12–1.31) (RMST and RMTL Ratios for each year in Supplementary Table S3). All RMSTD values and RMST/RMTL ratios at the observed time points were statistically significant ($p < 0.001$).

3.3 | Estimated RMSTD in OS for Patients With PC as Anastomotic Leakages

Regarding anastomotic leakage complications from eight articles [18–25] (Figure 2B, Table 2), the estimated RMSTD was −0.05 years (95% CI: −0.07, −0.03) at the 1-year follow-up, −0.14 years (95% CI: −0.19, −0.09) at the 2-year follow-up, −0.20 years (95% CI: −0.29, −0.12) at the 3-year follow-up, −0.27 years (95% CI: −0.38, −0.15) at the 4-year follow-up, and −0.34 years (95% CI: −0.49, −0.19) at the 5-year follow-up. Additionally, the RMST ratio was estimated to be 0.89 (95% CI: 0.85–0.94) at the 5-year follow-up, and the RMTL Ratio was estimated to be 1.64 (95% CI: 1.39, 1.93) at the 1-year follow-up and 1.19 (95% CI: 1.11, 1.28) at the 5-year follow-up. All RMSTD values and RMST/RMTL ratios at the observed time points were statistically significant ($p < 0.001$).

3.4 | Estimated RMSTD in OS for Patients With Pulmonary PCs

Regrading pulmonary PCs from four articles [18, 20, 28, 29] (Figure 2C, Table 2), the RMSTD and RMST/RMTL ratios indicated pulmonary PC may have a severer impact on long-term OS. The estimated RMSTD was −0.05 years (95% CI: −0.07, −0.03) at the 1-year follow-up, −0.19 years (95% CI: −0.24, −0.13) at the 2-year follow-up, −0.33 years (95% CI: −0.42, −0.23) at the 3-year follow-up, −0.48 years (95% CI: −0.62, −0.34) at the 4-year follow-up, and up to −0.63 years (95% CI: −0.81, −0.45) at the 5-year follow-up. Additionally, the RMTL Ratio was estimated to be 2.38 (95% CI: 1.82, 3.12) at the 1-year follow-up and 1.53 (95% CI: 1.36, 1.73) at the 5-year follow-up. All RMSTD values and RMST/RMTL ratios at the observed time points were statistically significant ($p < 0.001$).

4 | Discussion

The occurrence of PCs following esophagectomy remains a significant concern, with more than half of patients experiencing PCs [30]. This meta-analysis innovatively conducted a comprehensive assessment of the effects of overall PCs, anastomotic leakages, and pulmonary PCs on OS by RMSTD and RMST/RMTL ratios. Our findings indicate that PCs significantly reduced the long-term survival for patients, and this negative impact gradually intensified over time. This study updates the current evidence and has important clinical implications for the timely identification and treatment of PCs.

Our findings added new evidence to the effect of overall PCs on OS, and we estimated that the patients with overall PCs generally lived an average of 0.39 years shorter than those without PCs, or the survival time lost for patients with overall PCs was 1.21 times that of patients without PC at the 5-year follow-up. This result is consistent with previous studies. Bona et al. used the RMSTD method and found that patients with severe PCs (Clavien–Dindo grade > 3) lived 8.6 months less than those with no PCs or mild PCs (Clavien–Dindo grade = 1 or 2) [31]. This RMSTD was higher than our estimates, potentially because they focused on severe PCs, as well as this study classified patients with no PCs and mild PCs into a single reference group. A large-scale retrospective analysis found that PCs significantly increased the long-term mortality risk for esophageal cancer patients, particularly complications occurring within 30 days post-surgery, which were closely related to the 5-year survival rate [32]. This finding highlights that PCs are not only crucial for the short-term recovery of patients but also have a profound impact on their long-term survival. PCs may affect survival through various pathways, such as increasing postoperative inflammatory responses, leading to decreased immune function, which in turn promotes tumor recurrence or metastasis [33]. Additionally, PCs may result in treatment delays, such as the postponement or interruption of adjuvant therapy, further worsening the patient's prognosis [8]. A study also indicated that cancer-specific survival was significantly reduced in patients with PCs, supporting the clinical significance of our findings [34].

Anastomotic leaks are among the most common complications following esophagectomy, and their negative impact on long-term survival has been clearly validated in this study. We found that the RMSTD was −0.34 years at the 5-year follow-up, and we updated the previous meta-analysis. Aiolfi et al. estimated that the RMSTD was −0.35 years by using the studies by October 2022 [35]. Another study also showed that the occurrence of anastomotic leaks was closely related to poorer survival rates after esophageal cancer surgery and can serve as an independent adverse prognostic factor [36]. However, among eight studies we included, Kamarajah et al. (trial 5) showed results on the RMSTD curve results that were contrary to other studies [21]. This study used a single-center, high-volume data and found that anastomotic leak complications prolonged intensive care time but did not significantly impact long-term survival. Prior studies have indicated that in certain high-volume centers, due to the early screening and prevention, along with optimized management of patients, the impact of complications on long-term survival is mitigated [37]. The adverse impact of anastomotic leaks on survival may be attributed to multiple factors. First, anastomotic leaks are often accompanied by severe infections and systemic inflammatory responses, which may impair immune system function and increase the risk of cancer recurrence and metastasis [38]. Second, anastomotic leaks may lead to delays or interruptions in treatment, especially in patients requiring adjuvant radiotherapy and chemotherapy, further worsening patient

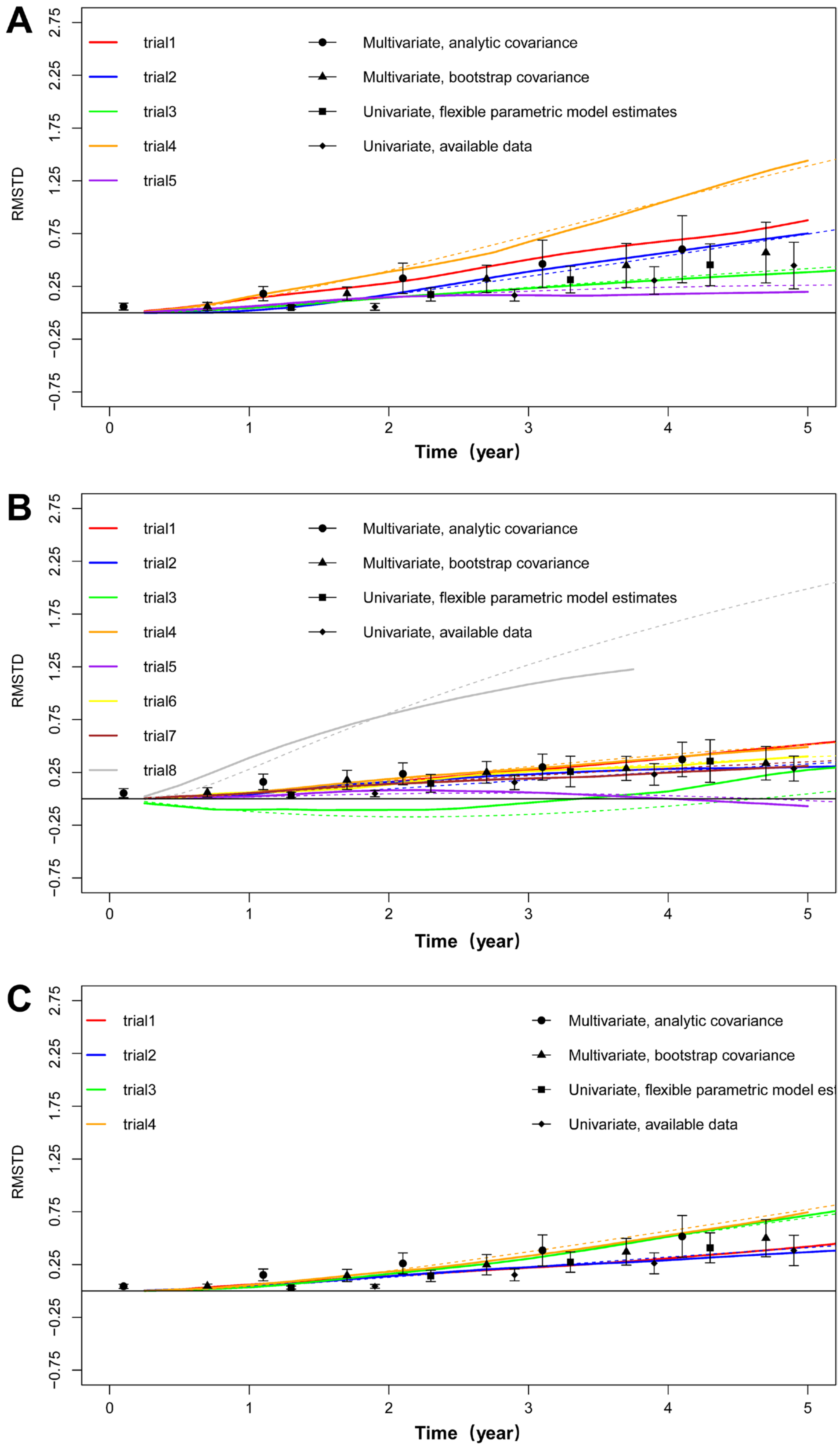

FIGURE 2 | Estimated RMSTD for overall, anastomotic leakage, and pulmonary PCs in patients following esophagectomy.

prognosis. Additionally, anastomotic leaks may also affect patients' nutritional status and overall physical health, which is one of the important reasons for the decline in long-term survival rates [8, 39]. More efforts are needed to provide early screening and prevention and timely treatment to reduce the adverse impact of anastomotic leaks and other PCs on survival.

TABLE 2 | Estimated RMSTD, RMST ratio, and RMTL ratio in patients following esophagectomy, stratified by the type of PCs.

		Types of PCs					
		Overall		Anastomotic leakage		Pulmonary	
	Follow-up check point (year)	Coefficient	95% CI	Coefficient	95% CI	Coefficient	95% CI
RMSTD	1	−0.04	(−0.06, −0.03)	−0.05	(−0.07, −0.03)	−0.05	(−0.07, −0.03)
	2	−0.14	(−0.19, −0.09)	−0.14	(−0.19, −0.09)	−0.19	(−0.24, −0.13)
	3	−0.23	(−0.32, −0.14)	−0.20	(−0.29, −0.12)	−0.33	(−0.42, −0.23)
	4	−0.31	(−0.43, −0.18)	−0.27	(−0.38, −0.15)	−0.48	(−0.62, −0.34)
	5	−0.39	(−0.55, −0.22)	−0.34	(−0.49, −0.19)	−0.63	(−0.81, −0.45)
RMST ratio	1	0.95	(0.93, 0.97)	0.95	(0.93, 0.97)	0.95	(0.93, 0.96)
	5	0.88	(0.83, 0.93)	0.89	(0.85, 0.94)	0.83	(0.79, 0.88)
RMTL ratio	1	1.54	(1.28, 1.84)	1.64	(1.39, 1.93)	2.38	(1.82, 3.12)
	5	1.21	(1.12, 1.31)	1.19	(1.11, 1.28)	1.53	(1.36, 1.73)

Abbreviations: PC: Postoperative complication; RMST: Restricted mean survival time; RMSTD: Restricted mean survival time difference; RMTL: Restricted mean time loss.

Our findings suggest that pulmonary complication had a relatively higher long-term impact on OS, and pulmonary complications reduced the average survival time of patients by 0.05 years at the 1-year follow-up, which was comparable to the short-term impact of anastomotic leaks, and by 0.63 years at the 5-year follow-up, nearly double the long-term impact of anastomotic leaks. A prior study reported that the RMSTD was −0.71 years at the 5-year follow-up based on 9 articles searched by February 2023 [34]. Our study updated these findings and added the RMST/RMTL ratios. Similarly, another study demonstrated that patients who developed pulmonary PCs had a significantly lower 5-year survival rate than those without complications [40]. A five-year follow-up study also observed that pulmonary complications had the most substantial impact on the survival of post-esophagectomy patients compared to other complications, such as anastomotic leaks, recurrent laryngeal nerve injury, and postoperative infections [20]. Common pulmonary complications include pneumonia, atelectasis, respiratory failure, bronchospasm, acute respiratory distress syndrome (ARDS), pneumothorax, pleural effusion, and pulmonary fibrosis. These complications not only affect short-term survival but may also influence the biological behavior of tumors through long-term inflammatory responses and immunosuppressive effects. For instance, persistent inflammatory responses may promote changes in the tumor microenvironment, increasing the risk of cancer recurrence [41, 42]. In the short term, pulmonary complications may lead to patient frailty, thereby limiting their ability to receive subsequent treatments [43]. Pulmonary complications can significantly impair respiratory function, increasing the risk of respiratory failure and mortality. In the long term, patients with pulmonary complications may experience one or more symptoms, such as cough, chest tightness, and shortness of breath, potentially exacerbating chronic respiratory diseases (e.g., pulmonary fibrosis) [41]. These patients are more likely to have a relatively low quality of life and become more vulnerable to any infection. Recurrent pulmonary infections and changes in the lung interstitium due to drug treatments, including steroids, can also lead to the development of interstitial lung disease, negatively affecting the long-term prognosis of patients [44].

Our findings have important implications for clinical practice. First, early prevention and timely management of PCs are essential strategies for improving patient prognosis. For example, perioperative optimization measures, such as enhanced nutritional support, rational use of antibiotics to prevent infections, and early pulmonary function rehabilitation training, may help reduce the incidence of complications [45]. Second, the application of minimally invasive surgical techniques is also worth further promotion. Research has shown that minimally invasive esophagectomy (MIE) has a lower complication rate and better long-term survival compared to traditional open surgery [46]. Bograd and Molena pointed out that MIE not only reduced PCs but also significantly improved patients' quality of life and long-term survival rates [47]. Therefore, future efforts should focus on enhancing training and dissemination of MIE techniques to further improve surgical quality and patient prognosis. Finally, for patients who have already developed complications, a multidisciplinary collaborative management strategy should be adopted [48]. For example, in the management of anastomotic leaks, early detection and intervention are crucial, which may include monitoring through imaging and laboratory tests, endoscopic treatment, interventional therapy, or surgical treatment [49]. For pulmonary complications, active respiratory rehabilitation, anti-infection treatment, and close monitoring should be conducted to reduce the adverse impact of complications on long-term survival [50].

Our findings provide evidence for the application of RMSTD to examine the effects of PCs on OS following esophagectomy. Our results may further validate the findings of several published systematic reviews, with discrepancies in absolute survival benefit analyses due to updates in the included literature. Additionally, we conducted a relative survival benefit analysis and reported both the RMST Ratios and the RMTL Ratios. Over the past decade, methodological advancements have led some studies to suggest that the ratio of RMTL or RMST in the intervention group compared to the control group can substitute for HR [9, 51]. Uno et al. evaluated the validity based on several clinical trials to support it [9]. However, more researchers are conservative and recommend using RMSTD analysis as a more detailed and advanced assessment method [52–54]. Therefore, there is a clear need to facilitate further discussion and validation of methodological guidance in the future.

This study has several limitations. First, we were unable to differentiate the capacities of the centers involved in the meta-analysis. In some high-capacity centers, the management by multidisciplinary teams and extensive treatment experience can often effectively improve short-term outcomes and reduce the mortality rate associated with complications. Second, the number of articles included in this meta-analysis was insufficient to support the subgroup analysis of specific types of anastomotic leaks and pulmonary complications. Different surgical methods are associated with varying incidences, types, and severity levels of PCs. For instance, MIE may reduce the PC incidence compared to open surgery. However, many of selected studies included more than one surgical method and did not distinguish the outcomes for the subtype of surgical methods or cancer types. More specific studies are necessary to improve homogeneity and provide precise information for clinical decision-making. Finally, although RMSTD has unique advantages in the long-term survival analysis, because it remains applicable when the proportional hazards assumption is not met, the clinical interpretation of its results must still be contextualized within specific circumstances. Future research should be based on the ECCG consensus and design high-quality, large-scale prospective studies according to the different subcategories of each complication to further validate the findings of this study and optimize postoperative management strategies, particularly in reducing the incidence of complications and improving patients' long-term survival rates.

Author Contributions

Y.B.Y. and H.Z. contributed to the study design, literature selection, data interpretation, and the drafting of the manuscript. C.Y.H. conducted literature searches, performed data analyses and interpretation, and drafted the manuscript. X.X. conducted data analyses and interpretation and revised the manuscript. L.L., Z.Q., and Q.N.W. conducted literature selection and revised the manuscript. All authors approved the final draft of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.