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A retrospective cohort study on radio/chemotherapy and survival following esophageal fistula in esophageal cancer patients with prior radiotherapy

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Abstract

Background/Objective Radiotherapy is a common treatment for patients with esophageal cancer. Esophageal fistula (perforation) is a serious complication in patients with advanced esophageal cancer. It is unclear how radio/chemotherapy post-fistula may affect survival in patients with malignant esophageal fistulae with radiotherapy pre-fistula. We sought to evaluate radio/chemotherapy and survival post-fistula in patients with esophageal cancer and radiotherapy pre-fistula.

Methods In a retrospective cohort study, we reviewed post-fistula treatments and survival in 98 patients with esophageal cancer and prior radiotherapy with or without chemotherapy between 2010/6 and 2023/5 in a regional cancer care centre in Zhengzhou, China. The primary outcome was survival time (months) post-fistula. The inverse of the probability of treatment weighting (IPTW) was applied in Cox regression models in assessing the association between post-fistula radio/chemotherapy and survival accounting for baseline clinical risk factors.

Results The median survival time post-fistula was 3.5 months (inter-quartile range: 1.4–7.8 months). Compared to patients without radio/chemotherapy post-fistula, longer survival was observed in patients with radiotherapy [adjusted HR 0.40 (95% CI 0.20–0.80)], chemotherapy [adjusted HR 0.24 (0.08–0.72)], or chemo and radiotherapy [adjusted HR 0.10 (0.05–0.19)] post-fistula. Among patients with radiotherapy post-fistula, longer survival was observed in patients with both chemo and radiotherapy [adjusted HR 0.18 (0.08–0.36)] than with radiotherapy only.

Conclusions In patients with malignant esophageal fistulae and radiotherapy pre-fistula, continued radiotherapy post-fistula may improve survival, and combined radio/chemotherapy may be beneficial to optimal survival.

Keywords Esophageal cancer, Esophageal fistula, Radio/chemotherapy, Prognosis, Survival

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Introduction

Esophageal cancer is the sixth most common cancer in China [1]. Esophageal fistula is a serious complication in patients with advanced esophageal cancer with a post-fistula median survival of 2 to 8 months [2–4]. Common management options for malignant esophageal fistulae include surgical resection, stent grafting, gastrostomy, nasogastric tube and conservative care, and any active management of fistula appears to be better than conservative care for survival prognosis in these patients overall [5, 6]. Radiotherapy is a common treatment (with or without chemotherapy) in patients with esophageal cancer. Radio/chemotherapy is effective in improving overall survival in patients with esophageal cancer [7, 8]. It remains unclear whether continued radiotherapy post-fistula may improve survival in patients with prior radiotherapy. Currently, there are no clear clinical guidelines concerning whether active radio/chemotherapy of the primary malignancy should continue after esophageal fistula in patients with esophageal cancer. It has been suggested that the management of patients with malignant esophageal fistulae should be limited to palliative care [9]. Nevertheless, real-world evidence studies suggest a survival benefit of radiotherapy and/or chemotherapy post-fistula in patients with malignant esophageal fistulae [3, 10–12]. Although there is limited evidence suggesting the potential benefits of radiotherapy and/or chemotherapy, the certainty of those findings is questionable due to their study designs and methods. A common limitation of previous studies is the lack of accounting for potential confounding in the selection of treatment options post-fistula in the analyses. Without proper statistical evaluation of confounders and effect modifiers, adjusting or removing their effect on the main model of treatment efficacy may not be ideal evidence to prepare clinical guidelines for treating the disease. In addition to these, the previous studies also lacked systematic comparisons among the patients who received no intervention vs. continued radio/chemotherapy or both [13, 14]. In the present study, we sought to evaluate whether radio/chemotherapy post-fistula affects survival in patients with esophageal cancer and prior radiotherapy accounting for the propensity in the selection of treatment options, using real-world evidence data from a regional tertiary cancer care center in Henan province, China.

Methods

Patients and data

This retrospective cohort study was conducted at Henan Provincial Cancer Hospital, affiliated with Zhengzhou University, China. The hospital is the largest regional cancer care center in Henan province. We identified all patients with esophageal cancer with esophageal fistula and radiotherapy pre-fistula with clinical care records available on treatments and survival post-fistula between 1 June 2010 and 30 May 2023 ($n = 98$). Esophageal fistula was diagnosed by esophageal endoscopic ultrasonography and barium meal oesophagography or chest CT scan. Demographic and clinical data were extracted from medical records, including age, sex, primary diagnosis of esophageal cancer, location of cancer (neck-upper chest, middle chest, lower chest), T4 stage (yes/no), radio/chemotherapy before fistula (radiotherapy only, sequential radio/chemotherapy, concurrent radio/chemotherapy), date and diagnosis of fistula, fistula type (esophagotracheal, esophagea-mediastinal), antibiotics use post-fistula (yes/no), fistula management (esophageal stent grafting, gastrostomy, nasogastric tube, conservative care), radio/chemotherapy post-fistula (radiotherapy only, chemotherapy only, chemo and radiotherapy, neither), date and survival status in the last clinical visit record.

The primary outcome was post-fistula survival time calculated as the interval between the date of diagnosis of esophageal fistula and the date of death or the last clinical care record if the patient remained alive. The primary exposure of interest is radio/chemotherapy post-fistula (radiotherapy only, chemotherapy only, chemo and radiotherapy, neither).

The study was approved by the research ethics board of Henan Cancer Hospital (ref. # 202003). Individual informed consent was waived as the study was a retrospective review of medical care records. There was no personally identifiable information in the final research data in the analyses.

Treatments before and after esophageal fistula

All esophageal cancer patients had received intensity-modulated radiotherapy, with or without platinum-based chemotherapy (sequential or concurrent), following the clinical practice guidelines of the Chinese Society of Clinical Oncology. There are no consensus treatment recommendations for fistulae in esophageal cancer patients. After the occurrence of esophageal fistula, anti-cancer treatment (radiotherapy and/or chemotherapy) was temporarily suspended, and adequate antibiotics were given to prevent or control infections. Subsequent esophageal fistula management options (esophagectomy, stent grafting, gastrostomy, nasogastric tube, conservative care) and anti-cancer treatment options (resuming radiotherapy and/or chemotherapy, or neither) are at the discretion of the treating physician and the patient on a case-by-case basis. Also, for the management of nutritional support for esophageal cancer with fistula, an artificial opening in the abdomen channelling the stomach was established. Patients were informed of the potential benefits and risks of fistula management options and continued radiotherapy and/or chemotherapy.

Statistical analysis

Continuous variables were described by median and inter-quartile range (IQR) or 95% confidence intervals (CI). Categorical variables were described by frequency and proportion (%). The median (95% CIs) of survival time was calculated using the Kaplan-Meier method. Kaplan-Meier curve was plotted to illustrate the difference in survival time by post-fistula radio/chemotherapy treatment options. The log-rank test was used to assess the differences in survival time across groups. To account for potential bias in the selection of post-fistula radio/chemotherapy treatment options (radiotherapy only, chemotherapy only, chemo and radiotherapy, neither) due to differences in baseline (pre-fistula) clinical risk factors, propensity score-based inverse probability of treatment weights (IPTW) were calculated by the TWANG (toolkit for weighting and analysis of non-equivalent groups) package in R [15] and were used in weighting the data in Cox regression models in estimating the adjusted hazard ratios (HR) of death. The propensity scores were based on a multivariate multinomial logit model. Fistula type, management, and radio/chemotherapy post-fistula were forced into the Cox models to predict survival post-fistula. In the selection of co-variables in multivariate models, only co-variables with P < = 0.2 were retained in the final parsimonious models. All statistical analyses were conducted in R studio. Two-sided P values < 0.05 were considered statistically significant.

Results

Of the 98 patients with radiotherapy, the median radiation dose was 40.0 Gy (IQR: 23.8–50.4 Gy). The median age of study patients was 63 years (IQR: 55–71), and 45.6% of patients were over 65 years. The majority of study patients were male (75.5%), and more than half of patients were at T4 stage (53.1%) (Table 1). Most patients had esophageal-mediastinal fistulae (60.2%). Nasogastric tube (51.0%) and gastrostomy (29.6%) were the most frequent fistula management options. Prior to fistula, 26 patents (26.5%) had radiotherapy only, and 72 patients (73.5%) had chemo and radiotherapy. Post-fistula, 16 patients (16.3%) had radiotherapy only, 10 patients (10.2%) had chemotherapy only, 20 patients (20.4%) had chemo and radiotherapy, while 52 patients (53.1%) did not take chemo or radiotherapy. Fistula closure was recorded in 44 (44.9%) patients, and was more frequently observed in patients with any radio/chemotherapy vs. patients without any radio/chemotherapy post-fistula (68.2% vs. 29.6%, $P < 0.001$).

Of the 98 patients with malignant esophageal fistulae, 88 died and 10 remained alive in the last clinical care record. The median survival time was 3.5 months (IQR: 1.3–12.0 months). Figure 1 presents the Kaplan-Meier survival curves in patients stratified by radio/chemotherapy post-fistula. Patients received either radiotherapy or chemotherapy post-fistula had better survival than patients who did not ($P < 0.001$), and those who received both chemo and radiotherapy had the best survival time. The median survival time post-fistula was 10 months in patients received chemo and radiotherapy, 4.8 months in those received radiotherapy only, 8.0 months in those received chemotherapy only, and 2.0 months in those did not receive radio/chemotherapy post-fistula (Table 1).

In crude association analyses, the median survival time post-fistula was shorter in patients over 65 years of age (median: 2.4 vs. 4.1 months, $P = 0.03$), and in patients with high blood leukocytes 0–7 days before the diagnosis of fistula (1.4 vs. 4.2 months, $P = 0.02$), but longer in patients with radiotherapy total dose ≥ the median (40 Gy) (5.2 vs. 2.0 months, $P < 0.001$), and in those who had subsequent fistula closure (6.0 vs. 2.0 months, $P < 0.001$) (Table 1). There were no significant differences in survival time by esophageal cancer pathological type (squamous cell, other), the location of the primary cancer (neck/upper chest, middle chest, lower chest), the use of antibiotics, fistula type (esophagotracheal vs. esophageal-mediastinal), fistula management (esophageal stent grafting, gastrostomy, nasogastric tube, conservative care), or moderate/severe anemia prior to fistula. Although there were no statistically significant differences in survival time post-fistula across fistula management options, the median survival post-fistula was the lowest in patients without active management of the fistula (conservative care, median survival 1.9 months). Females patients tended to have a longer survival time than males (4.6 vs. 3.1 months. $P = 0.10$).

Patient characteristics by radio/chemotherapy post-fistula treatment options are presented in Appendix Table S1. Patient's age (< 65, >=65 y), T4 stage (yes/no) and prior radio/chemotherapy (radiotherapy only, concurrent radio/chemotherapy, sequential radio/chemotherapy) were associated with post-fistula radio/chemotherapy treatment options, and were included in the model for the propensity scores (probabilities) of post-fistula radio/chemotherapy treatment options using the TWANG package in R.

In the propensity score-based IPTW multivariate cox regression analyses, the survival benefits remained in patients with radio/chemotherapy as compared with those without radio/chemotherapy post-fistula after accounting for the differences in baseline clinical characteristics. The adjusted HRs of death were 0.40 (95% CI 0.20–0.80) for patients receiving radiotherapy only, 0.24 (0.08–0.72) for patients receiving chemotherapy only, and 0.10 (0.05–0.19) for patients receiving chemo and radiotherapy, respectively (Table 2). Higher hazards of death were observed in patients at T4 stage (adjusted HR 2.32

Table 1 Patient characteristics and survival time (months) after esophageal fistula in patients with esophageal cancer ($n=98$)

Characteristic	*N* (%)	Survival (months)		Crude HR (95% CI)
		Median (95% CI)	*P* *	
Age (years)			0.03	
<65	53 (54.1)	4.1 (3.0–10.0)		Reference
≥65	45 (45.9)	2.4 (1.7-5.0)		1.21 (0.74–1.99)
Sex			0.10	
Male	74 (75.5)	3.3 (2.0–5.0)		Reference
Female	24 (24.5)	4.6 (1.3–23.0)		0.62 (0.45–1.85)
T4 stage			0.86	
No	46 (46.9)	4.0 (2.0-6.3)		Reference
Yes	52 (53.1)	3.0 (2.0–6.0)		1.47 (0.93–2.32)
Pathological type			0.52	
Squamous cell	96 (98)	3.5 (2.3-5.0)		Reference
Other	2 (2)	3.2 (1.5-NE)		0.88 (0.33–2.34)
Primary cancer's location			0.59	
Neck/upper chest	37 (37.8)	4.0 (2.3-6.0)		Reference
Middle chest	52 (53.1)	3.3 (2.0-6.3)		1.24 (0.75–2.05)
Lower chest	9 (9.2)	2.5 (1.5-NE)		0.95 (0.45–2.03)
Radio/chemotherapy before fistula			**0.01**	
Radiotherapy only	26 (26.5)	1.4 (1.0–4.0)		Reference
Concurrent radio/chemotherapy	39 (39.8)	5.5 (3.1–12.0)		0.49 (0.27–0.90)
Sequential radio/chemotherapy	33 (33.7)	4.2 (1.7-6.0)		0.79 (0.40–1.57)
Fistula type			0.20	
Esophageal-mediastinal	59 (60.2)	4.7 (3.0–6.0)		Reference
Esophagotracheal	39 (39.8)	2.3 (2.0–6.0)		1.37 (0.85–2.20)
Fistula management			0.86	
Esophageal stent grafting	7 (7.1)	5.0 (1.0-NE)		1.21 (0.40–3.65)
Gastrostomy	29 (29.6)	3.0 (2.0–12.0)		1.10 (0.51–2.35)
Nasogastric tube	50 (51.0)	4.0 (2.0-6.9)		1.04 (0.49–2.21)
Conservative care	12 (12.2)	1.9 (1.3-NE)		Reference
Radio/chemotherapy post-fistula			**< 0.001**	
Radiotherapy	16 (16.3)	4.8 (1.8–19.0)		0.45 (0.23–0.87)
Chemotherapy	10 (10.2)	8.0 (3.0-NE)		0.34 (0.14–0.85)
Radio and chemotherapy	20 (20.4)	10.0 (5.5-NE)		0.15 (0.09–0.27)
Neither	52 (53.1)	2.0 (1.3-4.0)		Reference
Radiotherapy total dose			< 0.001	
< Median	46 (46.9)	2.0 (1.5-4.0)		Reference
≥Median (40 Gy)	52 (53.1)	5.2 (3.3–12.0)		0.50 (0.30–0.85)
Fistula closure			**< 0.001**	
No	54 (55.1)	2.0 (1.3-4.0)		Reference
Yes	44 (44.9)	6.0 (4.7–12.0)		0.30 (0.19–0.46)
Antibiotics			0.37	
No	16 (16.3)	7.0 (2.0–19.0)		Reference
Yes	82 (83.7)	3.0 (2.0-4.8)		1.42 (0.63–3.17)
Blood test 0–7 days before fistula				
Leukocytes			**0.02**	
Normal	76 (77.6)	4.2 (3.0-6.3)		Reference
High (> $9.5*10^9$/L) £	22 (22.4)	1.4 (1.1-5.0)		2.23 (1.37–3.63)
Neutrophils			0.27	
Normal/low	69 (70.4)	4.2 (2.5–6.3)		Reference
High (> $6.3*10^9$/L) £	29 (29.6)	2.0 (1.3-5.0)		1.73 (1.08–2.79)
Lymphocytes			0.95	

Table 1 (continued)

Characteristic	*N* (%)	Survival (months)		Crude HR (95% CI)
		Median (95% CI)	*P* *	
Normal	36 (36.7)	3.3 (2.0-6.3)		Reference
Low (< $1.1*10^9$/L) [£]	62 (63.3)	4.0 (2.0–6.0)		0.97 (0.61–1.55)
Moderate/severe anemia			0.91	
No	80 (81.6)	4.0 (2.3-5.0)		Reference
Yes (< 10 g/dL)	18 (18.4)	3.0 (1.8–15.0)		1.29 (0.77–2.14)

* *P* values from log-rank tests for differences in survival time across different sub-groups; *P* values in bold, $P < 0.05$

[£] According to the reference values from the clinical biochemistry laboratory in the study hospital

HR, hazard ratio (from Cox regression); NE, not estimable

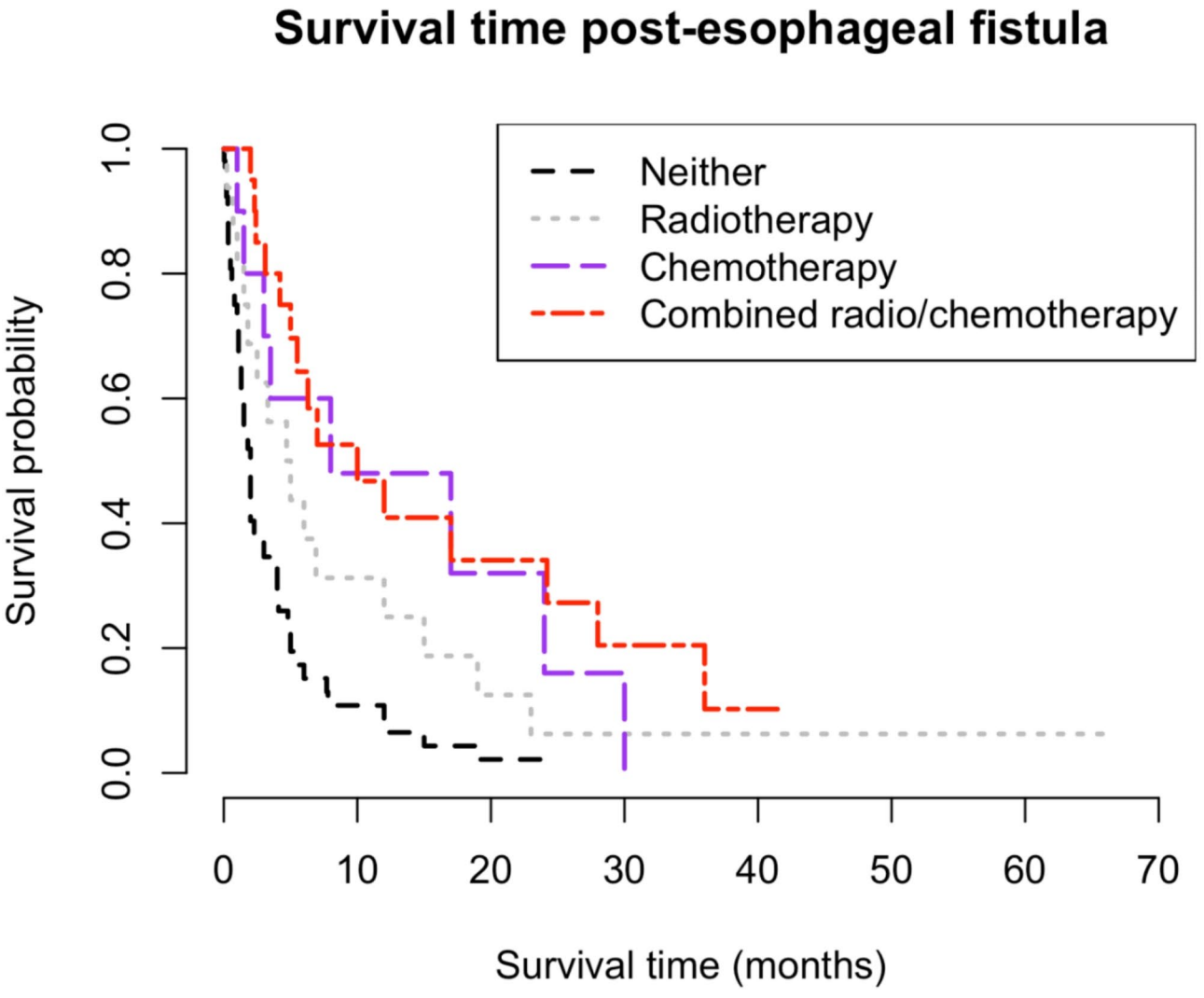

Fig. 1 Kaplan-Meier curves illustrating post-fistula survival time (in months) differences in patients with esophageal cancer by radio/chemotherapy post-fistula ($n = 98$); $P < 0.001$ in log-rank test for differences across the four strata

[1.35–3.99]), while lower hazards of death were observed in gastrostomy vs. conservative care (adjusted HR 0.41 [0.20–0.84]) in the management of esophageal fistula.

Among patients receiving radio/chemotherapy post-fistula, patients receiving chemo and radiotherapy had better survival than patients receiving radiotherapy only (adjusted HR 0.18 [0.08–0.36]) (Table 3). A similar survival benefit was observed in patients with chemotherapy only vs. radiotherapy only post-fistula (adjusted HR 0.17 [0.03–0.98]). Greater hazards of death were observed in

Table 2 Multivariate predictors of post-fistula survival in all study patients with esophageal cancer ($n=98$)

	HR (95% CI)	*P*
T4 stage	2.32 (1.35–3.99)	**0.016**
Fistula type		
Esophageal-mediastinal	Reference	
Esophagotracheal	1.33 (0.76–2.31)	0.31
Fistula management		
Conservative care	Reference	
Esophageal stent grafting	0.67 (0.24–1.86)	0.44
Gastrostomy	0.41 (0.20–0.84)	**0.01**
Nasogastric tube	0.61 (0.32–1.17)	0.14
Radio/chemotherapy post-fistula		
Neither	Reference	
Radiotherapy only	0.40 (0.20–0.80)	**0.01**
Chemotherapy only	0.24 (0.08–0.72)	**0.01**
Chemo and radiotherapy	0.10 (0.05–0.19)	**< 0.001**

*Data presented are the adjusted hazard ratios (HR) from a multivariate Cox model with inverse of the probability treatment weighting (IPTW) to account for the propensity (probability) of receiving radio/chemotherapy post-fistula. Fistula type, management and radio/chemotherapy post-fistula were forced into the model; only co-variables with P < = 0.2 were retained in the final parsimonious model

P values in bold: $P < 0.05$

Table 3 Multivariate predictors of post-fistula survival in esophageal cancer patients with radio/chemotherapy post-fistula ($n=46$)

	HR (95% CI)	*P*
Sex, male	9.13 (3.34-28.0)	**< 0.001**
Leukocytes 0–7 days before fistula		
Normal/low	Reference	
High (> $9.5*10^9$/L)	3.63 (1.31–10.1)	**0.01**
Fistula type		
Esophageal-mediastinal	Reference	
Esophagotracheal	1.87 (0.80–4.36)	0.15
Fistula treatment		
Conservative care	Reference	
Esophageal stent grafting	3.74 (1.20–11.6)	**0.02**
Gastrostomy	0.71 (0.21–2.36)	0.57
Nasogastric tube	1.27 (0.55–2.94)	0.58
Radio/chemotherapy post-fistula		
Radiotherapy only	Reference	
Chemotherapy only	0.17 (0.03–0.98)	**0.047**
Chemo and radiotherapy	0.18 (0.08–0.36)	**< 0.001**

Data presented are the adjusted hazard ratios (HR) from a multivariate Cox model with inverse of the probability treatment weighting (IPTW) to account for the propensity (probability) of receiving radio/chemotherapy post-fistula. Fistula type, management and radio/chemotherapy post-fistula were forced into the model; only co-variables with P < = 0.2 were retained in the final parsimonious model

P values in bold: $P < 0.05$

male patients (adjusted HR 9.13 [3.34-28.0]), in patients with high leukocytes 0–7 days before fistula (adjusted HR 3.63 [1.31–10.1]), and in patients with esophageal stent grafting in fistula management (adjusted HR 3.74 [1.20–11.6]).

Discussion

Esophageal fistula is a morbid complication of esophageal cancer and its treatment has been challenging. Apart from palliative care in the restoration of food/nutrient intakes, the use of radio/chemotherapy post-fistula is at the discretion of the treating physician since there are no clear clinical guidelines due to inadequate research data concerning whether the use of chemo or radiotherapy post-fistula confers a true benefit to patient outcomes. This real-world evidence study demonstrated that the use of chemo or radiotherapy post-fistula could be beneficial to survival in esophageal cancer patients with prior radiotherapy.

The median survival time was 3.5 months in esophageal cancer patients post-fistula in the study cohort, comparable to previous reports [2–4]. All the three treatment options - radiotherapy only, chemotherapy only, and combined radio/chemotherapy were associated with

more favourable survival than without any radio/chemotherapy post-fistula in esophageal cancer patients in the IPTW analysis accounting for potential confounding in the selection of radio/chemotherapy post-fistula due to differences in baseline clinical characteristics. The findings are consistent with the reported survival benefits of radiotherapy with or without chemotherapy post-fistula in previous studies without having accounted for the confounding effects in the selection of treatment options post-fistula in the analyses [3, 10–12]. Patients without any radio/chemotherapy post-fistula had a dismal median survival of 2.0 months in our study cohort. In contrast, the median survival time was more than doubled in those with radio/chemotherapy post-fistula (median: 4.8 to 10 months). It should be cautioned that the use of chemo/radiotherapy post-fistula may be dependent on both the patient's critical illness status, the discretion of the treating physician, and the patient's preference that could not be fully accounted for in the analysis. The true survival benefits could be smaller as part of the survival benefits might derive from unmeasured more favourable clinical factors/conditions in patients with radio/chemotherapy post-fistula. There are both risks and benefits of radio/chemotherapy post-fistula as the anti-cancer effects may be associated with both the closure of esophageal fistula, and the worsening or development of esophageal fistula [3, 11, 16]. Our study suggests that overall, continued radio/chemotherapy post-fistula may be beneficial to patient outcomes.

Among patients with radio/chemotherapy, we observed that chemotherapy only or chemo plus radiotherapy was associated with better survival than radiotherapy only. These results indicate that for patients who could sustain chemotherapy post-fistula, such chemotherapy with or without concurrent radiotherapy on the primary malignancy might remain beneficial to survival.

It has been proposed that patients with radiotherapy or chemotherapy may benefit from the closure or significant narrowing of the esophageal fistula [10, 11, 13, 14, 17, 18]. In our study, fistula closure was associated with better survival post-fistula in the crude association analysis but was not associated with survival after adjusting for other patient characteristics. Patients with fistula closure were more likely to have been treated by radio/chemotherapy post-fistula (68.2% vs. 29.6%), suggesting that radio/chemotherapy post-fistula could partly account for the association between fistula closure and post-fistula survival.

It has been shown that active management of esophageal fistula - stent grafting, gastrostomy or nasogastric tube, could be beneficial for survival than conservative supportive care in patients with malignant esophageal fistulae [5, 6]. Similarly, we observed numerically better median survival time in esophageal stent grafting, gastrostomy or nasogastric tube vs. conservative care in esophageal fistula management in the present study, although statistical significance was reached for gastrostomy only in the adjusted analysis. Surprisingly, stent grafting was associated with a greater hazard of death among patients with radio/chemotherapy post-fistula. Studies in other independent cohorts are warranted to confirm this observation.

As expected, T4 stage was associated with poorer survival post-fistula among patients with malignant esophageal fistulae overall, consistent with a previous report [5]. High leukocytes 0–7 days prior to the diagnosis of fistula was associated poorer survival among patients with radio/chemotherapy post-fistula, indicating a role of infection/inflammation in aggravating critical illness that may lead to fetal demise.

Our study has both strengths and limitations. The study was based on a real-world cohort of patients with malignant esophageal fistulae with data on radio/chemotherapy pre- and post-fistula. The use of the IPTW analysis could partly account for the confounding effects in the selection of post-fistula treatment options. The main limitation was its observational study nature; causal relationships could not be ascertained, and residual confounding could not be ruled out. Among all the participants, only one case of esophageal fistula occurred during chemoradiotherapy or radiotherapy and underwent salvage surgery. The patient survived for about one month post-operatively and died from infection. However, since the sample size of this study is already limited, we did not consider that patient to be exclusive to the other participants included in this study. All the study participants were Chinese and recruited from a single healthcare facility; therefore, this study's findings may not be generalizable to other racial or ethnic groups. More studies in other racial/ethnic groups are warranted to understand the generalizability of the study findings. In addition, since the study period was over 10 years, there may have been changes in healthcare providers, surgical techniques or treatment protocols, which might affect the consistency of the treatment procedure.

Conclusion

This real-world evidence study suggests a survival benefit of continued radiotherapy with or without chemotherapy post-fistula in patients with esophageal cancer and radiotherapy pre-fistula. Active anti-cancer radio/chemotherapy may remain to be recommended in esophageal cancer patients post-fistula if clinical conditions permit. The findings support a previous suggestion that esophageal fistula alone should not be a contraindication for radio/chemotherapy [11], and are in favour of the continued use of ant-cancer therapies in patients post-fistula when clinical conditions permit. A systematic review of similar studies in the published literature should be

conducted to highlight both the similarities and differences with the findings of this study. This review will also be crucial in providing a comparison of methodologies and will inform the guideline developer group to consider the unique contribution of this work.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12885-025-13853-2.

Supplementary Material 1

Author contributions

W.X. designed the study, conducted the data analyses, and wrote the manuscript. H.J., Y.L., X.L., and Y.J. collected the research data. All authors reviewed the manuscript.

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Data availability

Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate

The study was approved by the research ethics board of Henan Cancer Hospital (ref. # 202003).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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