Original Article

Effect of family history of cancer on postoperative survival in patients with non-small cell lung cancer

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Background: Family history of cancer (FHC) has been reported to increase mortality of non-small cell lung cancer, mainly comprised of lung adenocarcinoma (LUAD) and lung squamous cell carcinoma (LUSC). However, the impact of FHC on long-term survival remains controversial. This study aims to identify the impact of FHC on postoperative survival in LUAD and LUSC.

Methods: Patients underwent lung resection for LUAD or LUSC in West China Hospital from 2009 to 2021 were enrolled. The 5-year overall survival (OS), lung cancer-specific survival (LCSS) and progression-free survival (PFS) were compared between the patients with and without FHC. Multivariable Cox regression was also performed.

Results: A total of 6,253 patients were enrolled, including 5,685 LUAD and 568 LUSC. Altogether 18.9% (1,077/5,685) patients had FHC in LUAD, and 12.7% (72/568) patients had FHC in LUSC. In LUAD, the patients with FHC showed comparable survival compared with the patients without FHC regarding 5-year OS (87.9% *vs.* 86.5%, P=0.49), 5-year PFS (84.8% *vs.* 80.9%, P=0.06), and 5-year LCSS (89.2% *vs.* 88.0%, P=0.96). In LUSC, the patients with FHC had poorer survival compared with the patients without FHC according to 5-year OS (40.9% *vs.* 68.2%, P=0.007), 5-year PFS (42.3% *vs.* 66.2%, P=0.003), and 5-year LCSS (45.8% *vs.* 72.7%, P=0.003). Multivariate analyses indicated that FHC was an independent prognostic factor of OS, PFS, and LCSS in the patients with LUSC.

Conclusions: FHC was associated with a poor survival after lung resection in LUSC not LUAD patients. More attention should be paid in postoperative monitoring and treatment in LUSC patients with FHC.

Keywords: Family history of cancer (FHC); lung cancer; surgery; survival

Submitted Mar 26, 2024. Accepted for publication May 27, 2024. Published online Aug 21, 2024.
doi: 10.21037/tlcr-24-349
View this article at: https://dx.doi.org/10.21037/tlcr-24-349

Introduction

Lung cancer is the leading cause of cancer-related deaths worldwide, including non-small cell lung cancer (NSCLC), and small cell lung cancer (1). NSCLC mainly compromises of lung adenocarcinoma (LUAD) and lung squamous cell carcinoma (LUSC). Surgery is the only curative treatment regimen in patients with early-stage lung cancer. However, postoperative survival of lung cancer patients is not promising. Identifying prognostic factors and interfering timely are essential for improving survival.

Family history of cancer (FHC) is related to increased cancer mortality (2-5), and family history of lung cancer (FH-LC) is regarded as a risk factor of lung cancer carcinogenesis (1,6). Previous studies have reported that FHC is a prognostic factor in some solid tumors, such as breast cancer (7), colorectal cancer (8), and prostate

cancer (9). In LUAD patients, a previous study indicated that FH-LC had no impact on postoperative recurrence, while family history of non-lung cancer (FH-nLC) was associated with increased risk of recurrence and death (10). FH-LC was also reported to have no impact on postoperative survival (11). However, another study reported that lung cancer patients with FH-LC had a poorer outcome than those without (12).

Difference cancer type of FHC is correlated with different genomic features (10,13), which means FHC might have different prognostic effect on lung cancer with different histology type. In LUSC patients, familial aggregation has also been observed, and FHC has been identified as a risk factor of cancer onset and progression (14,15). However, few studies focused on the relationship between FHC and the prognosis of LUSC patients. We herein conducted this study to identify the effect of FHC on postoperative survival in the patients with LUAD or LUSC. We present this article in accordance with the STROBE reporting checklist (available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-349/rc).

Highlight box

Key findings

- In lung adenocarcinoma (LUAD), the patients with family history of cancer (FHC) showed comparable survival compared with the patients without FHC regarding 5-year overall survival (OS) (87.9% *vs.* 86.5%, P=0.49), 5-year progression-free survival (PFS) (84.8% *vs.* 80.9%, P=0.06), and 5-year lung cancer-specific survival (LCSS) (89.2% *vs.* 88.0%, P=0.96).
- In lung squamous cell carcinoma (LUSC), the patients with FHC had poorer survival compared with the patients without FHC according to 5-year OS (40.9% *vs.* 68.2%, P=0.007), 5-year PFS (42.3% *vs.* 66.2%, P=0.003), and 5-year LCSS (45.8% *vs.* 72.7%, P=0.003). Multivariate analyses indicated that FHC was an independent prognostic factor of OS, PFS, and LCSS in the patients with LUSC.

What is known and what is new?

- FHC could increase the risk of cancer occurrence. However, the impact of FHC on postoperative survival in LUAD and LUSC patients remains unclear.
- We found that FHC was associated with a poor OS, LCSS, and PFS in LUSC patients after lung resection. While no significant impact was found in LUAD patients.

What is the implication, and what should change now?

- FHC is an independent prognostic factor in LUSC patients after lung resection. More attention should be paid in postoperative monitoring and treatment in LUSC patients with FHC.

Methods

Study design and data source

This study was a retrospective cohort study of patients undergoing lung resection for LUAD or LUSC. The report of this study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology statement (16).

Patient data were gathered and extracted from a prospectively established database. This study was approved by the Ethics Committee of West China Hospital of Sichuan University (No. 2022-641), and the requirement for informed consent was waived due to the retrospective nature of this study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Population

The patients with LUAD or LUSC who underwent lung resection at the Department of Thoracic Surgery, West China Hospital between March 2009 and February 2021 were enrolled.

Inclusion criteria included: (I) older than 18 years old; (II) completing the self-reporting interview questions about their FHC; (III) pathological diagnosed with LUSC or LUAD; (IV) undergoing lung resection.

Exclusion criteria included: (I) emergency operations; (II) operations discontinued due to severe tumor adhesion; (III) identified as stage 0 by postoperative pathology; (IV) death within one month; (V) lack of detailed family history and follow-up information.

Data collection

Data collection included age, sex, smoking history, FHC, percentages for forced expiratory volume in 1 second of predicted values (FEV1%), percentages for diffusing capacity of the lungs for carbon monoxide of predicted values (DLCO%), comorbidity, type of surgery [video-assisted thoracic surgery (VATS) and thoracotomy], extent of resection (pneumonectomy, lobectomy, segmentectomy, wedge resection), clinicopathological feature of tumor (tumor size, pathological type, pathological stage), adjuvant therapy and FHC, as well as with survival data. FHC was defined as a self-reported FHC in first-degree (parents, offspring, siblings).

Outcomes

The primary outcome was overall survival (OS), defined as the date from lung cancer surgery to death or last follow-up. The secondary outcomes were progression-free survival (PFS) and lung cancer-specific survival (LCSS). PFS was calculated from the date of surgery until first relapse (radiologic findings or histologic confirmation) or death or the last follow-up. LCSS was defined as the interval between surgical resection to death owing to lung cancer other than other causes.

Treatment and follow-up

Preoperative evaluation for patients was mainly conducted through pulmonary function tests, high-resolution chest computed tomography (CT). All patients received anatomic lung resection and systematic or specific lymph node dissection, by VATS or thoracotomy. Three-port or uniportal VATS was performed using the single-direction thoracoscopic lobectomy technique as our center previously reported (17). Postoperative management and follow-up were conducted according to clinical practice. Follow-up method included outpatient visit, online clinic, and telephone.

Sample size estimation

Considering OS as the primary outcome, one prior literature reported that the quantity ratio of the FH-nLC and non-FHC was about 1:3, the hazard ratio (HR) of FH-nLC reached 1.65 compared to non-FHC (10). The alpha level was set as 0.05, with the power of the test of 0.9. The rate of loss of follow-up was assumed as 5%. Therefore, the minimal total sample size of this study would be 263 calculated by the software PASS (Version 15.0.5), with 65 cases in FHC group and 198 in non-FHC group.

Statistical analysis

The mean and standard deviation were used to describe measurement data with normal distribution. The median with interquartile range (IQR) was used to describe enumeration data. The former data would be analyzed using the Student's *t*-test while the latter would be analyzed using Pearson's chi-square test or Fisher's exact. OS, LCSS, and PFS were estimated via Kaplan-Meier method and survival curve was then plotted. Log-rank test was used to assess the survival difference between the groups. Univariate and multivariate analyses were performed through Cox regression model, with the HR and the corresponding 95% confidence intervals (CIs) calculated. All tests are two-sided tests. P value <0.05 was considered as statistically significant. All data were analyzed using R version 4.1.1 software (The R Foundation for Statistical Computing, 2021).

Results

Baseline characteristics

A total of 6,253 patients were enrolled, including 5,685 LUAD and 568 LUSC (*Figure 1*). Altogether 18.9% (1,077/5,685) patients had FHC in LUAD, and 12.7% (72/568) patients had FHC in LUSC. There was no significant difference of most baseline characteristics between two groups (*Table 1*). Only one relative has cancer was observed in 82.82% LUAD patients with FHC, while 91.67% LUSC patients with FHC (*Table 2*). The most frequent types of cancer were lung cancer, esophagus cancer, liver cancer, gastric cancer, and colorectal cancer.

Impact of FHC on survival

In LUAD, the patients with FHC showed comparable survival compared with the patients without FHC regarding 5-year OS [87.9% (95% CI: 83.9–92%) *vs.* 86.5% (95% CI: 84.4–88.7%), P=0.49] (*Figure 2A*), 5-year PFS [84.8% (95% CI: 80.8–88.9%) *vs.* 80.9% (95% CI: 78.8–83%), P=0.06] (*Figure 2B*), and 5-year LCSS [89.2% (95% CI: 85.6–93.1%) *vs.* 88.0% (95% CI: 85.9–90.2%), P=0.96] (*Figure 2C*).

In LUSC, the patients with FHC had poorer survival compared with the patients without FHC according to 5-year OS [40.9% (95% CI: 27.1–67.1%) *vs.* 68.2% (95% CI: 63–74.1%), P=0.007] (*Figure 3A*), 5-year PFS [42.3% (95% CI: 29.2–61.3%) *vs.* 66.2% (95% CI: 61.3–71.5%), P=0.003] (*Figure 3B*), and 5-year LCSS [45.8% (95% CI: 31.8–66%) *vs.* 72.7% (95% CI: 67.5–78.2%), P=0.003] (*Figure 3C*).

Multivariate analysis

In multivariate analysis, FHC was not an independent prognostic factor of OS (HR =1.11; 95% CI: 0.80–1.54; P=0.52), PFS (HR =0.96; 95% CI: 0.75–1.23; P=0.72), and LCSS (HR =1.23; 95% CI: 0.87–1.73; P=0.24) in the

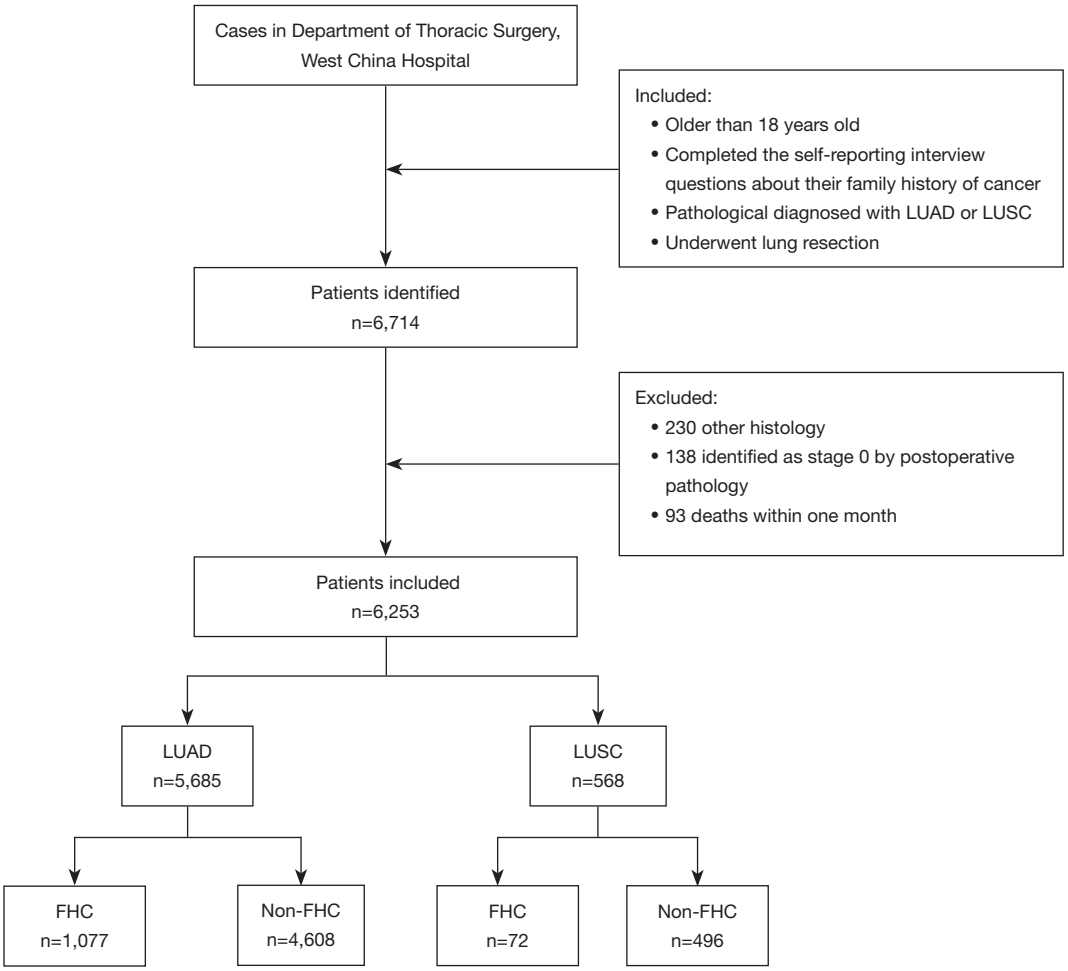

Figure 1 Flow chart of patient selection. LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; FHC, family history of cancer.

patients with LUAD (Table S1).

While FHC was found to be an independent prognostic factor of OS (HR =2.16; 95% CI: 1.35–3.44; P=0.001), PFS (HR =2.06; 95% CI: 1.34–3.17; P=0.001), and LCSS (HR =2.32; 95% CI: 1.42–3.78; P=0.001) in the patients with LUSC (Table S2).

Discussion

Our study indicated that LUSC patients who had a FHC in a first-degree relative experienced a negative impact on their survival following lung resection, not only on OS, but also on LSCC and PFS. While no significant impact of FHC was observed in LUAD patients.

Several previous studies have reported the association between FHC and prognosis of lung cancer. The study from Ganti *et al.* showed that the patients with lung cancer tended to get worse OS outcomes if they had relatives with cancer, specifically first-degree relatives (12). However, other studies reported the contrary results. Li *et al.* reported that patients with positive FHC were diagnosed at earlier age and at more advanced tumor stage than patients without FHC, but had decreased risk of death (18). Isla *et al.* also reported a higher median OS of FHC group than non-FHC group in the Spanish women cohort (19). There are some possible explanations for why several studies indicated that FHC would improve prognosis for patients with lung cancer. One might be that patients would concern more about good living habits like staying away from smoking if their relatives have developed cancer. People may also be more sensitive to smoke especially second- or third-hand smoke if their co-resident or relatives have a smoking habit.

Table 1 Baseline characteristics of the patients with or without family history of cancer

Characteristics	LUAD			LUSC		
	FHC (n=1,077)	Non-FHC (n=4,608)	P value	FHC (n=72)	Non-FHC (n=496)	P value
Age (years)	56.39 (9.35)	57.03 (11.36)	0.09	59.33 (7.65)	60.99 (9.51)	0.16
Sex						
Female	676 (62.77)	2,833 (61.48)	0.46	4 (5.56)	37 (7.46)	0.73
Male	401 (37.23)	1,775 (38.52)		68 (94.44)	459 (92.54)	
Smoking status			0.82			0.19
Current/ever	254 (23.58)	1,069 (23.20)		66 (91.67)	422 (85.08)	
Never	823 (76.42)	3,539 (76.80)		6 (8.33)	74 (14.92)	
FEV1%	105.79 (15.88)	105.18 (17.19)	0.30	91.96 (17.94)	89.24 (19.16)	0.28
DLCO%	101.12 (16.93)	100.93 (16.60)	0.75	92.52 (18.06)	92.25 (19.48)	0.92
CCI	0.17 (0.48)	0.17 (0.50)	0.91	0.38 (0.64)	0.29 (0.57)	0.23
VATS						
Open	15 (1.39)	108 (2.34)	0.07	25 (34.72)	152 (30.65)	0.57
VATS	1,062 (98.61)	4,500 (97.66)		47 (65.28)	344 (69.35)	
Resection extent			0.005			0.97
Pneumonectomy	1 (0.09)	7 (0.15)		4 (5.56)	24 (4.84)	
Lobectomy	596 (55.34)	2,786 (60.46)		64 (88.89)	447 (90.12)	
Segmentectomy	374 (34.73)	1,344 (29.17)		2 (2.78)	10 (2.02)	
Wedge resection	106 (9.84)	471 (10.22)		2 (2.78)	15 (3.02)	
Size (cm)	1.73 (1.12)	1.84 (1.19)	0.008	3.51 (1.81)	3.92 (2.09)	0.13
Pathological stage			0.30			0.11
I	947 (87.93)	3,952 (85.76)		29 (40.28)	197 (39.72)	
II	47 (4.36)	259 (5.62)		30 (41.67)	156 (31.45)	
III	74 (6.87)	360 (7.81)		12 (16.67)	141 (28.43)	
IV	9 (0.84)	37 (0.80)		1 (1.39)	2 (0.40)	
Adjuvant chemotherapy	134 (12.44)	562 (12.20)	0.87	36 (50.00)	242 (48.79)	0.95
Adjuvant radiotherapy	19 (1.76)	84 (1.82)	>0.99	4 (5.56)	39 (7.86)	0.65
Targeted therapy	63 (5.85)	305 (6.62)	0.39	1 (1.39)	5 (1.01)	>0.99

Data were presented as mean (SD) or number (percentage). LUAD, lung adenocarcinoma; FHC, family history of cancer; LUSC, lung squamous cell carcinoma; FEV1, forced expiratory volume in 1 second; DLCO, diffusing capacity of the lungs for carbon monoxide; CCI, Charlson comorbidity index; VATS, video-assisted thoracic surgery; SD, standard deviation.

Another possible explanation is that the patients with FHC receive earlier cancer screening, which leads to an earlier diagnosis (8,20,21). An early diagnosis could contribute to better quality of treatment and cure (22). Nevertheless, one cohort study suggested that there was no difference on tumor staging between the patients with FHC and without FHC, hence more clues are needed to explain the beneficial impact of FHC.

Of noting, the aforementioned studies enrolled the patients with great heterogeneity, such as various pathological types (NSCLC and small cell lung cancer) and treatment regimens (surgery, radiotherapy, chemotherapy).

Table 2 Family history of cancer in LUAD and LUSC patients

Characteristics	LUAD with FHC (n=1,077)	LUSC with FHC (n=72)
Number of relatives with cancer, n (%)		
1	892 (82.82)	66 (91.67)
≥2	185 (17.18)	6 (8.33)
Relationship, n (%)		
Father and mother	84 (7.80)	3 (4.17)
Father and mother and siblings or offspring	16 (1.49)	0 (0.00)
Father and siblings or offspring	41 (3.81)	1 (1.39)
Father only	498 (46.24)	42 (58.33)
Mother and siblings or offspring	38 (3.53)	2 (2.78)
Mother only	273 (25.35)	20 (27.78)
Siblings or offspring only	121 (11.23)	4 (5.56)
Others[†]	6 (0.56)	0 (0.00)
Type of cancer[‡], n (%)	n=892	n=66
Lung	434 (48.65)	28 (42.42)
Esophagus	97 (10.87)	13 (19.70)
Liver	81 (9.08)	7 (10.61)
Gastric	67 (7.51)	6 (9.09)
Colorectum	61 (6.84)	3 (4.55)
Pancreas	23 (2.58)	1 (1.52)
Breast	18 (2.02)	2 (3.03)
Lymphoma	11 (1.23)	0 (0.00)
Nasopharynx	11 (1.23)	0 (0.00)
Blood	10 (1.12)	1 (1.52)
Gallbladder	9 (1.01)	1 (1.52)
Prostate	8 (0.90)	0 (0.00)
Bladder	7 (0.78)	1 (1.52)
Ovary	7 (0.78)	0 (0.00)
Brain	6 (0.67)	0 (0.00)
Larynx	6 (0.67)	0 (0.00)
Uterus	6 (0.67)	0 (0.00)
Oral	5 (0.56)	2 (3.03)
Thyroid	5 (0.56)	0 (0.00)
Kidney	4 (0.45)	0 (0.00)
Bone	3 (0.34)	0 (0.00)
Cervix	3 (0.34)	0 (0.00)
Rectum	2 (0.22)	0 (0.00)
Mediastinal	1 (0.11)	0 (0.00)
Melanoma	1 (0.11)	0 (0.00)
Meninx	1 (0.11)	0 (0.00)
Unknown	5 (0.56)	1 (1.52)

[†], grandparents and cousins; [‡], in patients with only one relative developing cancer. LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; FHC, family history of cancer.

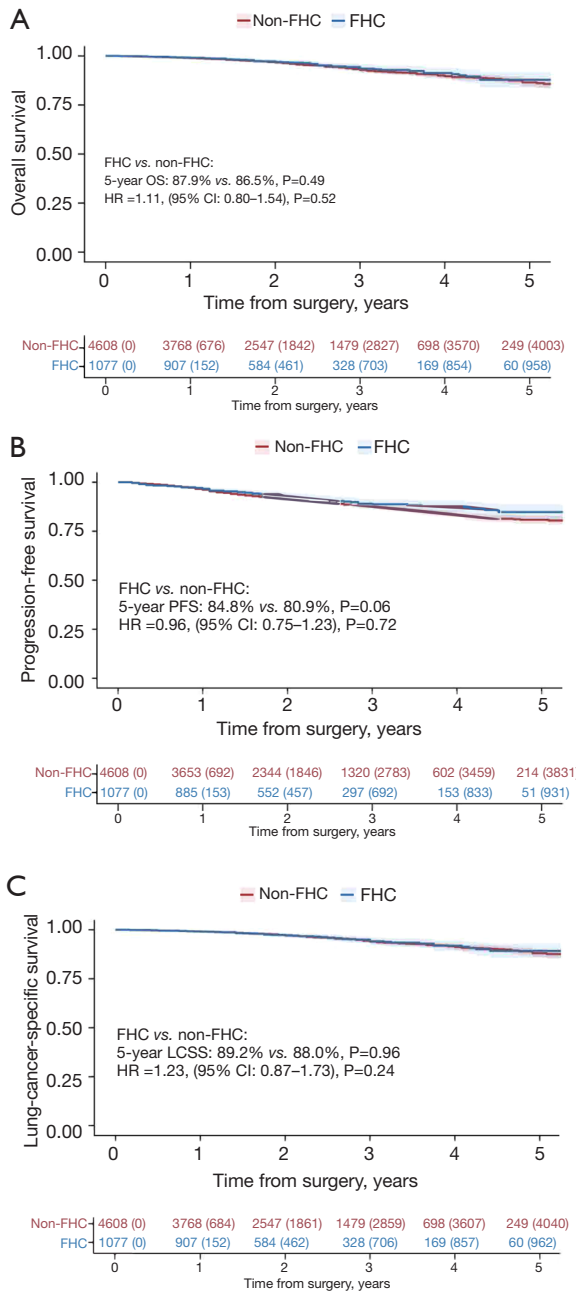

Figure 2 Kaplan-Meier survival curves for patients with and without FHC in LUAD patients after lung resection. (A) OS. (B) PFS. (C) LCSS. FHC, family history of cancer; OS, overall survival; HR, hazard ratio; CI, confidence interval; PFS, progression-free survival; LCSS, lung cancer-specific survival; LUAD, lung adenocarcinoma.

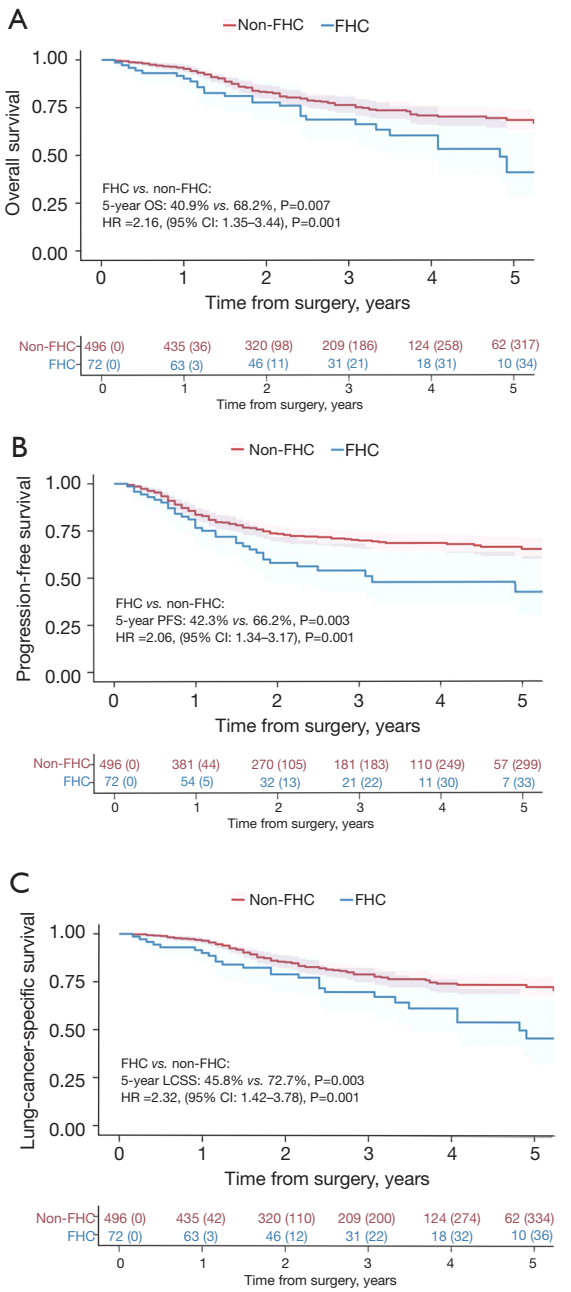

Figure 3 Kaplan-Meier survival curves for patients with and without FHC in LUSC patients after lung resection. (A) OS. (B) PFS. (C) LCSS. FHC, family history of cancer; OS, overall survival; HR, hazard ratio; CI, confidence interval; PFS, progression-free survival; LCSS, lung cancer-specific survival; LUSC, lung squamous cell carcinoma.

Given that surgery is the main curative treatment for lung cancer (1), it is important to reassess the prognostic impact of FHC in patients undergoing lung cancer surgery.

In this study, we found that FHC was an independent prognostic factor for survival of patients with LUSC in our study. Lee *et al.* enrolled 604 female never-smoking patients with LUAD after lung resection and found that the patients whose first-degree relatives had ever developing non-lung cancer would be exposed to higher risks of recurrence and death (10). However, the reason for detrimental effects of FHC on survival has not been elucidated clearly until now. We concluded four potential reasons: genetic differences, health-related behavior, shared environmental factors, and occurrence of second primary cancers. Firstly, given that in patients with NSCLC or other many cancers, an increasing number of significant germline mutations are identified in thoracic malignancy (23), prostate cancer (24), blood malignancy (25), and so forth. These germline mutations are more frequent in FHC group and might be associated with worse survival (26,27). Microsatellite instability and gene methylation level are also considered to be related to FHC and prognosis in colorectal cancer (28). However, few studies explore whether there is significant hereditary difference in lung cancer patients with FHC and if this is also associated with associated with long-term survival after surgery. Some studies analyzed the tumor genotype in lung cancer patients and found that epidermal growth factor receptor (EGFR) mutation (10,13) and anaplastic lymphoma kinase (ALK)/c-ros oncogene 1 (ROS1)/ rearranged during transfection (RET) fusions (10) were significantly associated with FHC. A parametric genetic linkage analysis suggested that regions on chromosomes 12q, 7p, and 4q might increase the risk of occurrence of familial clustered lung cancers (29). Another worth noting concern is the clonal hematopoiesis mutations. It has been recently reported that FH-LC is a strong risk factor of clonal hematopoiesis mutations, and clonal hematopoiesis mutations may affect the immune response of the body to tumor (30). Secondly, patients with FHC might keep the same harmful living habits as their relatives with cancer. In this study, we found more smokers in the patients with FHC. Still as we discussed earlier, the change of living habits, for better or worse, would not uniform in the certain group of patients with FHC. Thirdly, Renkonen *et al.* (31) found that siblings and spouses of head and neck cancers patients were at a higher risk of developing head and neck cancers, denoting the significant role of shared environmental factors. Cluster onset of cancer might partly indicate common exposure to significant adverse factors, and might be associated with worse survival to some extent (31). Furthermore, recent publications are taking an interest in the association between FHC and second primary cancer. FHC has been reported to be significantly associated with occurrence of second primary cancers in patients with Hodgkin lymphoma (32), ovarian cancer (33), breast cancer (34), prostate cancer (35), and squamous cell skin cancer (36), and second primary cancers have deleterious effect on survival (37).

The impact of FHC on survival was different in the patients with LUAD and LUSC. We should note that there were more males in LUSC and more females in LUAD in our cohort. Furthermore, more early stage was in LUAD compared with that in LUSC. Female and early stage are regarded as good prognostic factors in lung cancer after surgery. In recent years, numerous studies have highlighted the distinct biological mechanisms underlying LUSC and LUAD are different, leading to diverse clinical prognosis (38,39). Chen *et al.* (38) identified a higher prevalence of TP53 mutations in LUSC patients. Meanwhile, a previous study demonstrated a significantly higher rate of TP53 mutations in patients with FHC compared to those without FHC (40). Hence, we speculate that the differential overlapping genes between LUAD/LUSC and the gene sets related to FHC might contribute to the disparate prognostic impact of FHC. In addition, smoking has been proved to be an independent risk factor for the onset of various cancers (41). Clinical evidence shows that compared with LUAD, the prognosis of LUSC are more closely related to smoking (42). Therefore, FHC may be more closely related to the prognosis of LUSC patients through its association with smoking environment. Nevertheless, there is currently a paucity of studies investigating the mechanism underlying the varied prognostic effects of FHC, necessitating further exploration. Moreover, we should be cautious when drawing conclusions regarding LUSC due to the limited sample size in our study.

Our findings might add to a growing body of evidence that suggests FHC plays a negative role in survival, not only in OS, but also in LCSS and PFS in LUSC patients after surgery. Clinicians need to pay more attention on family history of patients. Cancer screening for other family members is recommended in case of suspected familial aggregation (6). In addition, for patients with FHC, we should pay more attention to postoperative monitoring and timely treatment during follow-up. Lastly, our study revealed that FHC is an independent prognostic factor

in LUSC, prompting the question of whether individuals with FHC, who are suitable for sublobar resection, might experience greater benefits from undergoing lobectomy instead. Moreover, there is a need for further investigation into the clinical significance of incorporating perioperative treatments for high-risk NSCLC patients, particularly those with FHC.

There are some inevitable limitations needed to be clarified. Firstly, this is a retrospective study, leading to some ineluctable bias. Secondly, sample size was limited when analyzing the impact of FHC on LUSC patients. Further, we could not thoroughly discuss the association between genetic changes and FHC and how family history affects survival. Lastly, the role of postoperative treatment, especially immunotherapy and targeted therapy, in this scenario should be further explored. Further experiment study is needed to explore the mechanisms behind the survival impact of FHC and confirm the hereditary effect of FHC.

Conclusions

In LUSC patients after surgery, FHC could detrimentally affect OS, LCSS and PFS. No significant impact was observed in LUAD patients after surgery. It is significant to intensify the follow-up for patients with FHC. More large cohort studies and experimental studies are required to further explore the role of FHC and its mechanism in cancer onset and progression.

Acknowledgments

Funding: This work was supported by National Natural Science Foundation of China (No. 82102968 to J.Z., No. 82302624 to M.L.).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-349/rc

Data Sharing Statement: Available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-349/dss

Peer Review File: Available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-349/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tlcr.amegroups.com/article/view/10.21037/tlcr-24-349/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by the Ethics Committee of West China Hospital of Sichuan University (No. 2022-641). The requirement for informed consent was waived due to the retrospective nature of this study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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Cite this article as: Zhou J, Zheng Q, Huang Y, Lyu M, Wang T, Wu D, Liao H. Effect of family history of cancer on postoperative survival in patients with non-small cell lung cancer. Transl Lung Cancer Res 2024;13(8):1851-1861. doi: 10.21037/tlcr-24-349