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The clinical value of genetic testing in lung squamous cell carcinoma: A retrospective study

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Abstract

Objectives

To assess the necessity and clinical value of genetic testing in lung squamous cell carcinoma (LSCC) diagnosis and treatment.

Methods

This retrospective study enrolled 1,515 LSCC patients from Chongqing University Cancer Hospital. Medical records were reviewed to analyze gene mutations, treatment and healthcare economic outcomes for clinical benefit evaluation.

Results

Of 1,515 patients, 292 received genetic testing (221 smokers, 71 non-smokers). Fifty-six had clear driver gene mutations, with a 19.2% detection rate, dominated by EGFR (n = 26) and MET (n = 10) mutations. In non-smokers, the incidence of EGFR mutations (66.7%, 20/30) was significantly higher than that of other mutations, while the mutation types were scattered in smokers. Patients aged ≤ 65 years, females and non-smokers showed higher mutation rates. Targeted therapy improved objective response rate, disease control rate and median progression-free survival, with fewer grade 3–4 adverse events (4.7% vs 40.0%). Cost-effectiveness analysis showed a negative incremental cost-effectiveness ratio, meaning targeted therapy delivered better outcomes at lower costs.

Conclusions

Genetic testing is highly recommended for LSCC patients, especially non-smokers, those aged ≤ 65 years and females. Its combination with targeted therapy offers significant clinical benefits and favorable cost-effectiveness, guiding treatment selection and prognosis improvement.

Introduction

Lung cancer, as the malignant tumor with the highest incidence and mortality rate in China, poses a major challenge to public health. It causes severe physical and psychological suffering in patients and their families and imposes a heavy burden on the public healthcare system (Zheng 2024). In the diagnosis and treatment of lung cancer, the relatively mature precision therapy for lung adenocarcinoma has been established. Genetic testing has become one of the routine clinical examinations for this subtype, with its driver gene mutation rate reaching around 60% (Cancer Genome Atlas Research Network 2014). Based on the result of genetic testing, clinicians can formulate targeted therapy regimens for patients. This approach not only markedly improves treatment efficacy but also has less impact on patients' quality of life due to

mild adverse events (AEs). Moreover, it results in lower systemic damage compared with traditional chemoradiotherapy.

However, genetic testing has not been established as a routine examination for lung squamous cell carcinoma (LSCC) domestically or internationally. Previous studies have suggested limited clinical value of genetic testing in LSCC because of its low overall mutation rate and the absence of definite driver gene mutations in patients with a long smoking history (Reuss 2025). In recent years, several studies indicate that non-smoking patients with LSCC exhibit a higher incidence of driver gene mutations, and the progression of carcinogenesis in this subgroup may be more likely associated with such mutations (Murphy 2025).

In this study, we performed a retrospective analysis of 1,515 patients diagnosed with LSCC at Chongqing University Cancer Hospital to evaluate the clinical value of genetic testing in LSCC. Subgroup and cost-effectiveness analyses were also conducted, aiming to provide more comprehensive evidence-based medical data for the precision diagnosis and treatment of LSCC.

Methods

Study population

In this retrospective study, 1,515 patients with histopathologically confirmed LSCC treated at Chongqing University Cancer Hospital from January 2018 to December 2024 were included. Clinical data were collected for all patients, including sex, age, smoking status (smoking was defined as smoking ≥ 1 cigarette per day for at least 6 months; non-smoking was defined as never smoking or a cumulative smoking duration of < 6 months), pathological stage, genetic testing results, treatment regimens, treatment outcomes, quality-of-life assessments, and AEs. This retrospective study was approved by the Ethics Committee of Chongqing University Cancer Hospital (Approval No. CZLL2025-226-002). Informed consent was waived due to the use of fully anonymized clinical data.

Gene mutation analysis

Genetic testing was conducted on tumor tissues or body fluids using the amplification refractory mutation system (ARMS).

Treatment

After evaluating the patient's condition and communicating fully with the patient and their family, patients with identified gene mutations were prescribed corresponding targeted drugs. For the remaining patients with gene mutations but without corresponding targeted drugs, as well as those with no detectable gene mutations, conventional chemoradiotherapy regimens were administered until disease progression or death.

Outcomes assessment

All patients were scheduled for follow-up once a month after diagnosis. They received re-examination if any symptoms of disease progression occurred during treatment. The last follow-up was conducted in December 2025. And the median follow-up time was 20.0 months (range: 1.0–77.0 months). Tumor response assessment was performed according to the Response Evaluation Criteria in Solid Tumors (RECIST 1.0) and categorized into complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD). Objective response rate (ORR) was defined as the proportion of patients achieving CR or PR. Disease control rate (DCR) was defined as the proportion of patients achieving CR, PR, or SD. Progression-free survival (PFS) was defined as the period from diagnosis to disease progression, death, or the last follow-up. Overall survival (OS) was defined as the period from diagnosis to death, or the last follow-up. Meanwhile, quality-of-life scores, psychological scores, and recurrence/metastasis status of the patients were recorded before and after treatment.

Safety assessment

AEs of grade ≥ 1 occurring during treatment were documented and categorized into grades 1–4 according to the severity. The incidence of AEs and the proportion of treatment discontinuations due to AEs were calculated for each treatment subgroup.

Cost-effectiveness analysis

The costs of testing and treatment were calculated based on the medical charging standards of Chongqing City in 2024, including the cost of genetic testing, the average monthly cost of targeted drugs, and conventional chemotherapy. After insurance reimbursement, the self-payment was approximately 9000 RMB, 4931.5 RMB, and 15078.3 RMB, respectively. The quality-adjusted life year (QALY) and the incremental cost-effectiveness ratio (ICER) were calculated, using three times the per capita gross domestic product (GDP) of China as the cost-effectiveness threshold.

Statistical analysis

Statistical analyses were performed with the SPSS package (version 19.0, IBM, USA). Survival analysis was conducted with the Kaplan-Meier method. Chi-square test was used to compare mutation detection rates, as well as tumor response rates, AEs incidence between different treatment groups, and subgroup mutation rates. Statistical significance was set at $P < 0.05$.

Results

Gene mutation analysis

A total of 1,515 patients with LSCC were included in this study, among whom 292 underwent genetic testing (221 smokers and 71 non-smokers; 268 males and 24 females). The mean age was 65.2 years (range, 39.0–92.0 years). Definite driver gene mutations were identified in 56 of the 292 patients, with an overall

mutation detection rate of 19.2%. Stratified by smoking status, the mutation rate was 11.8% in smokers and 42.3% in non-smokers.

Among patients with detected mutations, *EGFR* mutation was identified in 26 cases, *MET* mutation in 10 cases, *ERBB2* mutation in 5 cases, *ROS1* mutation in 5 cases, *ALK* mutation in 4 cases, *NRAS* mutation in 4 cases, and *RET* mutation in 2 cases (Table 1). In non-smokers, the incidence of *EGFR* mutation (66.7%, 20/30) was significantly higher than that of other gene mutations, whereas mutation types in smokers were more scattered.

Subgroup analysis showed that the mutation detection rate was significantly higher in patients aged ≤ 65 years (20.6%, 29/141) than in those aged > 65 years (17.9%, 27/151). In terms of gender stratification, the mutation rate in female patients (70.8%, 17/24) was significantly higher than that in male patients (14.6%, 39/268; χ^2=44.99, P < 0.001). And the mutation rate in non-smoking patients (42.3%, 30/71) was significantly higher than that in smoking patients (11.8%, 26/221; χ^2=32.23, P < 0.001).

Table 1
Statistics of baseline characteristics and mutation status in patients with positive genetic test results

Number	Genotype	Sex	Age	Smoking Status
01	ALK	Male	81	Smoking*
02	ALK	Male	64	Smoking
03	ALK	Male	66	Smoking
04	ALK	Male	56	Smoking
05	EGFR	Male	61	Non-smoking**
06	EGFR	Male	85	Smoking
07	EGFR	Male	72	Non-smoking
08	EGFR	Male	74	Smoking
09	EGFR	Female	71	Non-smoking
10	EGFR	Male	69	Non-smoking
11	EGFR	Female	65	Non-smoking
12	EGFR	Female	54	Non-smoking
13	EGFR	Male	56	Smoking
14	EGFR	Male	67	Non-smoking
15	EGFR	Male	69	Non-smoking
16	EGFR	Female	65	Non-smoking
17	EGFR	Female	69	Non-smoking
18	EGFR	Male	52	Smoking
19	EGFR	Female	55	Non-smoking
20	EGFR	Male	63	Non-smoking
21	EGFR	Male	58	Smoking
22	EGFR	Female	72	Non-smoking
23	EGFR	Male	53	Non-smoking
24	EGFR	Female	64	Non-smoking
25	EGFR	Female	71	Non-smoking
26	EGFR	Female	74	Non-smoking
27	EGFR	Female	58	Non-smoking

Number	Genotype	Sex	Age	Smoking Status
28	EGFR	Male	91	Non-smoking
29	EGFR	Male	64	Smoking
30	EGFR	Female	59	Non-smoking
31	ERBB2	Male	72	Non-smoking
32	ERBB2	Male	83	Smoking
33	ERBB2	Male	60	Smoking
34	ERBB2	Female	76	Non-smoking
35	ERBB2	Male	61	Smoking
36	MET	Male	62	Non-smoking
37	MET	Male	55	Smoking
38	MET	Female	70	Non-smoking
39	MET	Female	59	Non-smoking
40	MET	Male	63	Smoking
41	MET	Male	71	Smoking
42	MET	Male	73	Non-smoking
43	MET	Female	92	Non-smoking
44	MET	Male	71	Smoking
45	MET	Male	65	Smoking
46	NRAS	Male	66	Smoking
47	NRAS	Male	68	Smoking
48	NRAS	Male	62	Non-smoking
49	NRAS	Male	69	Smoking
50	RET	Female	74	Non-smoking
51	RET	Male	60	Smoking
52	ROS1	Male	69	Smoking
53	ROS1	Male	64	Smoking
54	ROS1	Male	76	Smoking
55	ROS1	Male	55	Smoking
56	ROS1	Male	58	Non-smoking

* Smoking was defined as smoking ≥ 1 cigarette per day for at least 6 months

** Non-smoking was defined as never smoking or a cumulative smoking duration of < 6 months

Efficacy analysis

As of the last follow-up date (December 2025), among the 21 patients receiving targeted therapy, 4 achieved CR, 4 PR, 6 SD, and 7 PD, corresponding to an ORR of 38.1% and a DCR of 66.7%. The median PFS was 28.0 months (Fig. 1). Among the 35 patients receiving conventional therapy, 3 achieved CR, 4 PR, 4 SD, and 24 PD. ORR and DCR were 20.0% and 31.4%, respectively. Of these 35 patients, 11 remained progression-free, with a median PFS of 14.0 months (Fig. 1).

The efficacy of targeted therapy corresponding to different gene mutation subtypes is shown in Table 2. Among patients with EGFR mutations, targeted therapy was administered in 13 cases, achieving a DCR of 69.2% (9/13) and a mean OS of 34.8 months. In contrast, conventional therapy was given to 13 cases, with a DCR of 38.5% (5/13) and a mean OS of 33.2 months.

Long-term survival analysis demonstrated a mean OS of 30.0 months and a median OS of 28.0 months in the targeted therapy group. In contrast, the conventional therapy group had a mean OS of 23.4 months and a median OS of 14.0 months. The differences in OS between the two groups were statistically significant ($P < 0.05$). Analysis of recurrence and metastasis revealed that the recurrence rate was 33.3% (7/21) in the targeted therapy group, including 2 cases of local recurrence and 5 cases of distant metastasis (predominantly brain metastasis). In the conventional therapy group, the recurrence rate was 68.6% (24/35), including 9 cases of local recurrence and 15 cases of distant metastasis (predominantly bone and intrapulmonary metastasis). The risk of distant metastasis was significantly lower in the targeted therapy group (HR = 0.31, 95% CI: 0.13–0.72, P = 0.007).

Differences in quality-of-life and AEs between treatment groups

Quality-of-life and psychological scores were assessed for all patients before and after treatment during regular follow-up. The results indicated that the clinical benefits of patients receiving targeted therapy were significantly superior to those receiving conventional therapy (Table 2).

In the targeted therapy group (n = 21), the most common AEs were rash (38.1%) and diarrhea (28.6%), with the incidence of grade 3–4 AEs being only 4.7% (1/21, grade 3 rash [n = 1]). In the conventional therapy group (n = 35), the most common AEs were myelosuppression (65.7%) and gastrointestinal reactions (60.0%), with the incidence of grade 3–4 AEs being 34.3% (12/35, grade 3 myelosuppression [n = 8] and grade 3 nausea and vomiting [n = 4]). The proportion of treatment discontinuations due to AEs was significantly lower in the targeted therapy group (4.8%) than that in the conventional therapy group (34.3%; $\chi^2=6.42$, P = 0.011; Table 2).

Table 2
Therapeutic efficacy under different treatment options

Serial No.	Treatment group	Dead status	Tumor response assessment	Overall survival (Months)	Progression-free survival (Months)	Adverse reaction grade	Quality of life assessment*
C01	Conventional therapy	Alive	Complete response	54	54	1	1-1-1-1-1
C02	Conventional therapy	Alive	Complete response	77	77	1	1-1-1-2-1
C03	Conventional therapy	Alive	Complete response	47	47	1	1-1-1-1-1
C04	Conventional therapy	Alive	Partial response	16	16	1	1-1-1-1-2
C05	Conventional therapy	Alive	Partial response	14	14	2	1-1-1-2-2
C06	Conventional therapy	Dead	Partial response	62	62	1	1-1-1-2-1
C07	Conventional therapy	Dead	Partial response	9	9	1	1-1-1-2-1
C08	Conventional therapy	Dead	Stable disease	13	13	2	1-1-1-2-2
C09	Conventional therapy	Alive	Stable disease	28	28	1	1-1-1-2-1
C10	Conventional therapy	Dead	Stable disease	66	66	1	1-1-1-2-1
C11	Conventional therapy	Alive	Stable disease	20	20	2	1-1-2-2-2
C12	Conventional therapy	Alive	Progressive disease	26	3	3	1-1-1-2-3
C13	Conventional therapy	Dead	Progressive disease	9	5	3	1-1-2-3-2
C14	Conventional therapy	Dead	Progressive disease	8	1	3	2-2-3-2-2
C15	Conventional therapy	Dead	Progressive disease	2	2	3	1-2-2-1-3
C16	Conventional therapy	Dead	Progressive disease	6	4	4	1-2-3-2-3
C17	Conventional therapy	Dead	Progressive disease	30	13	2	1-1-1-2-2
C18	Conventional therapy	Dead	Progressive disease	5	1	3	1-2-3-2-2

Serial No.	Treatment group	Dead status	Tumor response assessment	Overall survival (Months)	Progression-free survival (Months)	Adverse reaction grade	Quality of life assessment*
C19	Conventional therapy	Dead	Progressive disease	3	2	3	2-2-3-2-2
C20	Conventional therapy	Dead	Progressive disease	7	4	2	1-2-2-2-1
C21	Conventional therapy	Dead	Progressive disease	14	10	3	1-2-2-3-1
C22	Conventional therapy	Dead	Progressive disease	60	13	1	1-1-2-2-1
C23	Conventional therapy	Dead	Progressive disease	11	7	1	1-1-2-1-1
C24	Conventional therapy	Dead	Progressive disease	2	2	4	2-2-3-3-2
C25	Conventional therapy	Dead	Progressive disease	20	16	2	1-1-1-2-2
C26	Conventional therapy	Dead	Progressive disease	8	2	2	1-1-2-2-2
C27	Conventional therapy	Dead	Progressive disease	19	3	4	2-2-3-4-3
C28	Conventional therapy	Alive	Progressive disease	44	2	4	2-2-3-3-2
C29	Conventional therapy	Dead	Progressive disease	55	23	1	1-1-2-2-1
C30	Conventional therapy	Dead	Progressive disease	3	1	4	2-2-3-4-3
C31	Conventional therapy	Dead	Progressive disease	2	1	4	2-2-3-4-3
C32	Conventional therapy	Dead	Progressive disease	8	4	2	1-1-2-2-2
C33	Conventional therapy	Dead	Progressive disease	1	1	2	1-1-2-2-2
C34	Conventional therapy	Dead	Progressive disease	8	4	3	1-1-2-3-3
C35	Conventional therapy	Alive	Progressive disease	61	4	1	1-1-1-1-1
T01	Targeted therapy	Alive	Complete response	20	20	1	1-1-1-1-2
T02	Targeted therapy	Alive	Complete response	68	68	1	1-1-1-1-1

Serial No.	Treatment group	Dead status	Tumor response assessment	Overall survival (Months)	Progression-free survival (Months)	Adverse reaction grade	Quality of life assessment*
T03	Targeted therapy	Dead	Complete response	34	34	1	1-1-1-1-1
T04	Targeted therapy	Alive	Complete response	15	15	1	1-1-1-1-1
T05	Targeted therapy	Dead	Partial response	35	35	2	1-1-2-1-2
T06	Targeted therapy	Alive	Partial response	19	19	1	1-1-1-1-1
T07	Targeted therapy	Alive	Partial response	56	56	2	1-1-1-2-2
T08	Targeted therapy	Alive	Partial response	30	30	1	1-1-1-1-1
T09	Targeted therapy	Dead	Stable disease	28	28	1	1-1-2-1-1
T10	Targeted therapy	Dead	Stable disease	16	16	1	1-1-1-1-1
T11	Targeted therapy	Dead	Stable disease	33	33	1	1-1-2-1-1
T12	Targeted therapy	Dead	Stable disease	28	28	1	1-1-1-1-1
T13	Targeted therapy	Dead	Stable disease	33	33	1	1-1-1-1-1
T14	Targeted therapy	Dead	Stable disease	11	11	1	1-1-2-1-1
T15	Targeted therapy	Dead	Progressive disease	17	14	1	1-1-1-1-2
T16	Targeted therapy	Dead	Progressive disease	3	3	3	1-1-2-3-3
T17	Targeted therapy	Alive	Progressive disease	26	2	2	1-1-2-2-1
T18	Targeted therapy	Dead	Progressive disease	27	16	2	1-1-2-2-1
T19	Targeted therapy	Alive	Progressive disease	61	24	1	1-1-2-1-1
T20	Targeted therapy	Alive	Progressive disease	43	31	1	1-1-2-1-1
T21	Targeted therapy	Alive	Progressive disease	28	17	1	1-1-1-2-1

** Health-related quality of life (HRQoL) was evaluated in this study using the EQ-5D-5L questionnaire, with corresponding scores obtained across five ordered dimensions: Mobility(MO), Self-care(SC), Usual activities(UA), Pain/discomfort(PD), and Anxiety/depression(AD).*

Cost-effectiveness analysis

The QALY was 2.287 in the targeted therapy group and 1.534 in the conventional therapy group. The ICER exhibited a negative value, indicating that targeted therapy yielded more favorable health outcomes with lower treatment costs. As an absolutely dominant strategy, it possessed a significant cost-effectiveness advantage. Collectively, these findings indicate that genetic testing combined with targeted therapy confers a favorable cost-effectiveness profile in non-smoking patients with LSCC.

Discussion

As one of the major subtypes of lung cancer, LSCC is a consistent challenge in clinical diagnosis and treatment due to its high invasiveness and low response rate (Bray 2018; Zheng 2024). Currently, the standard treatments for LSCC primarily include chemotherapy and radiotherapy. Although these conventional approaches can control tumor progression to some extent, they also compromise patients' quality of life (Garon 2015; Fernandes 2023). Their drug toxicity and radiation-induced damage harm normal tissues, leading to severe AEs such as myelosuppression and gastrointestinal reactions. Moreover, conventional therapy is associated with the risk of tumor recurrence and metastasis, which further poses a challenge to patients' quality of life. In addition, while the use of immune checkpoint inhibitors has shown efficacy in some patients, the ORR remains below 20%, which is insufficient to meet the clinical needs (Shim 2017).

Targeted therapy guided by genetic testing is an intervention method that targets specific molecular sites of tumor cells (Bouchard 2025; Jeon 2025). It specifically inhibits tumor cell proliferation and reduces damage to normal tissues (Jaiyesimi 2024; Su 2025). Compared with conventional therapy, it has the advantages of milder side effects and better tolerability, which exert a more positive impact on patients' quality of life (Attili 2023). The results of this study demonstrated that patients with LSCC receiving targeted therapy experienced early relief of symptoms such as cough, hemoptysis, and dyspnea caused by tumor compression or invasion, which significantly improved their physical condition and quality of life scores. These benefits may be attributed to the relatively milder adverse reactions and the precision of targeted therapy. In this study, the incidence of grade 3–4 AEs in the targeted therapy group was only 4.7%, significantly lower than that in the conventional therapy group (34.3%), further confirming the safety advantage of targeted therapy.

Previous clinical studies on the efficacy of targeted therapy for lung adenocarcinoma have shown that the ORR can be increased by 2–3 fold, and the median OS can be extended by 6–12 months in treated patients relative to the control group (Mok 2017). There is a gap in the efficacy of targeted therapy for LSCC compared with lung adenocarcinoma, largely due to its underutilization in the former. Promoting genetic testing, particularly among non-smoking patients with LSCC, is expected to narrow this gap (Niu 2022). In this study, the overall mutation detection rate in patients with LSCC reached 19.2%, with a significant

difference between the smoking (11.8%) and non-smoking (42.3%) groups. However, the current rate of genetic testing in patients with LSCC (19.3%, 292/1515) remains at a low level in clinical practice. This can be attributed to three reasons. First, the previous notion holds that LSCC is a non-mutation-driver tumor with a lower mutation rate compared to lung adenocarcinoma. Second, the mutation spectrum of LSCC related to smoking is complex and lacks clear and highly frequent mutations that can serve as targets (Heist 2012). Third, there are debates regarding the cost-effectiveness ratio between testing expenses and clinical benefits, which has also limited the routine implementation of genetic testing in clinical practice to some extent.

The findings of this study indicated that although the overall mutation rate in LSCC was relatively low, group analysis revealed that the gene mutation rate in non-smoking patients was significantly higher than that in smoking patients, with more prominent mutation characteristics observed in non-smoking females aged ≤ 65 years with advanced-stage disease. The underlying mechanisms for this phenomenon may be directly related to the differences in carcinogenic factors, DNA repair capacity, and disease-driving pathways (Lu 2024). First, the primary carcinogenic drivers in smoking patients with LSCC are a small subset of highly recurrent smoking signature mutations (such as *TP53*) induced by polycyclic aromatic hydrocarbons (such as benzopyrene) in tobacco (Denissenko 1996). Their tumor progression relies more on non-mutation-driven factors like chronic inflammation and oxidative stress, resulting in a lower dependence on gene mutations (Forder 2023). In contrast, the pathogenic factors for non-smoking patients involve multiple elements, such as secondhand smoke, air pollution, occupational exposures, and genetic susceptibility, with their driver mutations covering a variety of genes, such as *EGFR*, *ALK*, and *ROS1* (Murphy 2025). Non-smoking patients with LSCC often exhibit a greater dependence on genetic mutations as the core driving events, with more diverse mutation types and a higher overall mutation proportion (Huang 2016). Second, defects in DNA repair-related genes such as *ERCC1* and *BRCA* are more common in non-smoking patients, which impairs the capacity for DNA damage repair and results in the failure to timely eliminate abnormal mutations (Azuma 2007). This leads to the accumulation of abnormal mutations and increases the detectable mutation rate. This discovery provides a theoretical foundation for the implementation of precision therapy in non-smoking, younger, and advanced-stage patients with LSCC.

Conventional detection methods only target a few genes, such as *EGFR*. With the development of high-throughput sequencing technology, next-generation techniques like multi-gene panel testing can simultaneously cover multiple potential targets, including *ALK*, *ROS1*, and *MET*, significantly enhancing the detection capability for gene mutations in LSCC (Lindquist 2017). Related studies have shown that multi-gene panel testing can increase the comprehensive mutation detection rate by over 30%, creating opportunities for more patients to access targeted therapy (Illei 2017). At the same time, the accelerated development of targeted drugs for rare mutations has further expanded the clinical value of genetic testing.

The healthcare economic analysis revealed that the ICER of the targeted therapy group was negative, which was below the threshold of three times the per capita GDP in China obviously. The finding addresses cost-related concerns in clinical adoption and demonstrates that genetic testing combined with targeted therapy offers favorable health economic value for non-smoking patients with LSCC. It provides economic justification for the routine clinical implementation of this approach.

A comparison of the 2024 edition of the NCCN Clinical Practice Guidelines in Oncology for Lung Cancer and the CSCO Guidelines for the Diagnosis and Treatment of Non-Small Cell Lung Cancer reveals that both currently recommend genetic testing for *EGFR*, *ALK*, and *ROS1* in patients with LSCC who are non-smokers or light smokers (Category recommendation)(Riely 2024). However, potential targets such as *MET* and *RET* are not included. Based on the findings of this study, we suggest that the scope of genetic testing for non-smoking patients with LSCC should be expanded to cover multiple genes, including *EGFR*, *ALK*, *ROS1*, *MET*, *RET*, *ERBB2*, and *NRAS*. For smoking patients with advanced LSCC who are intolerant to conventional chemotherapy, next-generation sequencing (NGS)-based multi-gene testing may still be considered to explore additional treatment opportunities (Zhao 2022).

This study is limited by its single-center retrospective design. Future multicenter, prospective studies are therefore warranted to dynamically monitor the evolution of gene mutations during treatment. Additionally, collecting data on patients' health insurance payment types and treatment costs could further validate the long-term cost-effectiveness of genetic testing, thereby providing higher-level evidence for optimizing precision diagnosis and treatment guidelines for LSCC.

With the advancement of detection technologies and the development of targeted therapies, the era of precision therapy for LSCC has gradually arrived. Expanding the application of genetic testing in clinical practice, particularly for patients characterized by non-smoking status, younger age, and advanced disease stages, holds significant guiding value for treatment strategy selection and outcomes. Therefore, it is necessary to gradually enhance the awareness of the value of genetic testing among both clinicians and patients, and promote the transition of LSCC diagnosis and treatment from empirical medicine to precision medicine.

Declarations

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Jun Fang, Haiping Huang, Lin Xiong and Huiwen Ma. The first draft of the manuscript was written by Jun Fang and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data Availability

The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Chongqing University Cancer Hospital (Date 2025.12.02/No. CZLL2025-226-002).

Consent to participate

Informed consent was waived by the Ethics Committee of Chongqing University Cancer Hospital in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.

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Figures

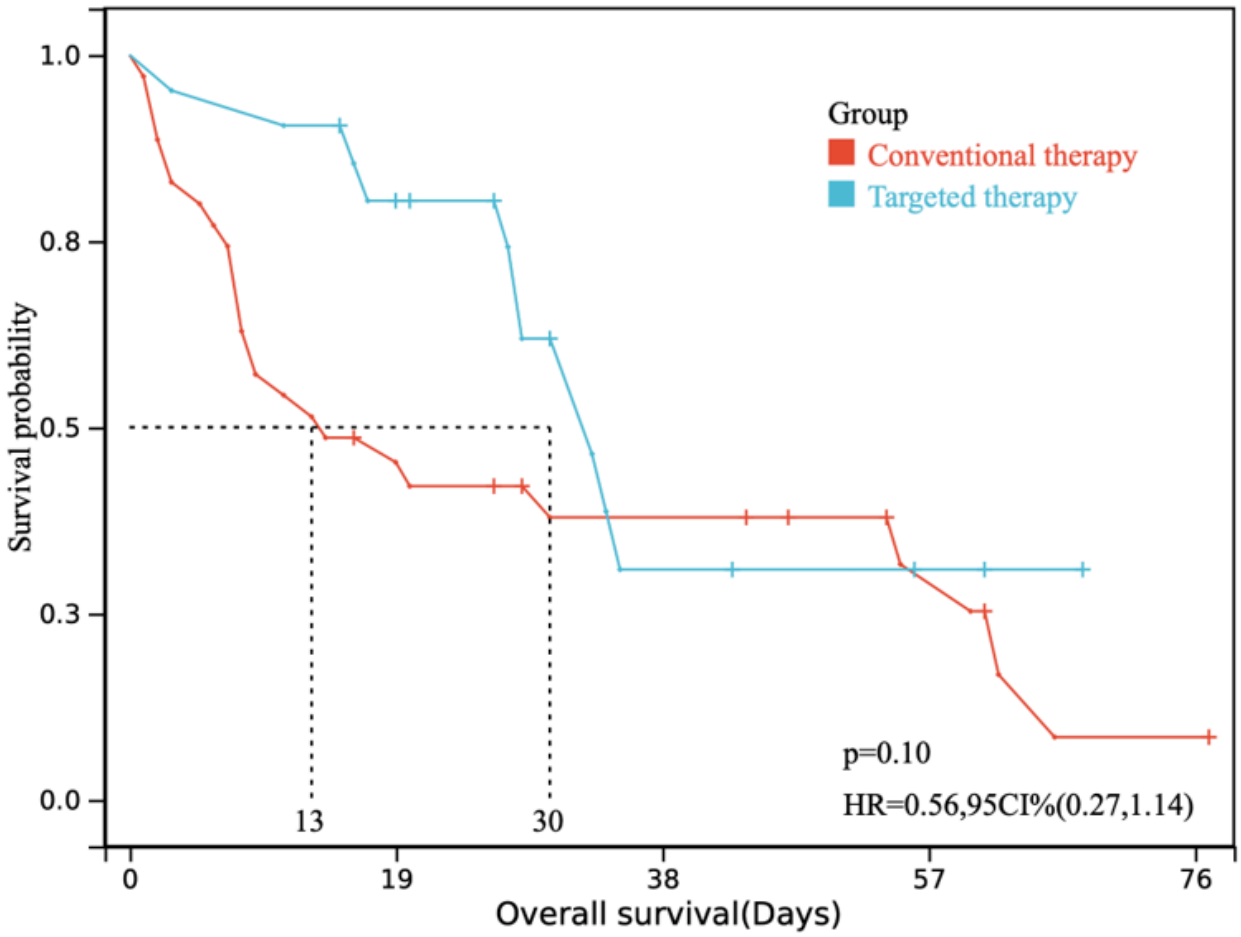


Figure 1

Survival curves for different treatment modalities