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Leukocyte telomere length serves as the novel prognostic biomarker for the resectable NSCLC

Guanxuan Chen[1], Shiwen Wang[2,3], Xinkai Mo[2], Wanqi Zhu[4], Ruoyu Wang[1]✉ & Xingguo Song[2,5]✉

The relationship of Leukocyte telomere length (LTL) dynamic changes with resectable NSCLC progression remains unclear. This study aims to reveal its clinical utility for prognosis of the resectable NSCLC. LTL was measured in 76 resectable NSCLC patients and 80 healthy controls using peripheral blood samples. Pre-operation LTL (Pre-LTL) and post-operation LTL (Po-LTL) were analyzed in relation to TNM stage, metastasis, and survival outcomes. The prognostic value was evaluated by disease-free survival (DFS) and overall survival (OS). NSCLC patients had significantly shorter LTL compared to controls, with LTL inversely correlated to disease stage. Po-LTL increased significantly and was associated with better OS. Combining Po-LTL with TNM stage improved prognostic prediction for OS and DFS. LTL is a promising biomarker for predicting prognosis in resectable NSCLC. Po-LTL, as well as in combination with TNM stage, enhances predictive accuracy for OS and DFS.

Keywords Leukocyte telomere length (LTL), Resectable NSCLC, Prognosis, Biomarker, Telomerase reverse transcriptase (TERT)

Non-small cell lung cancer (NSCLC) is the most common cancer, with a 3-year survival rate of just 40%[1], posing a major health risk. Surgical resection remains the most efficacious treatment modality for patients with stage I–II NSCLC and select cases of stage IIIA, with 5-year survival rates ranging from 56 to 90% for those with stage I–II disease[2–4]. Nevertheless, the absence of specific symptoms during the early stages of NSCLC often results in diagnosis at more advanced or metastatic stages. Furthermore, a considerable proportion of patients experience recurrence or metastasis following surgical intervention, culminating in treatment failure and significantly impacting prognosis[2]. Therefore, the identification of early markers for post-operation recurrence and metastasis in NSCLC is a crucial challenge.

Telomeres, composed of non-coding DNA repeat sequences and protein complexes that cap the ends of chromosomes, are essential structures for maintaining the stability and function of eukaryotic chromosomes. In normal cells, telomeres gradually shorten with each cell division. When they reach a critical length, the cells stop dividing or enter a state of senescence, thereby preserving chromosome stability. However, during tumorigenesis, in response to the cellular crisis induced by telomeres shortening, cells often counteract this by reactivating telomerase (telomerase reverse transcriptase, TERT) or employing mechanisms such as alternative lengthening of telomeres (ALT) to elongate telomeres[5]. These processes enable the cells to acquire the capacity for unlimited proliferation, a hallmark of cancer.

Telomere length is a promising biomarker for cancer risk[5–7]. Studies have shown significant individual variability in telomere length[8], with a strong correlation between telomere length in various somatic tissues, so individuals with long telomere length in one tissue typically exhibit long telomere length in other tissues. This synchrony also extends to blood cell telomere length, making it a reliable indicator across different[9]. Consequently, leukocyte telomere length (LTL) is often used as a surrogate for other tissues to explore the relationship between individual telomere length and disease risk. Both longer and shorter telomeres are associated with increased cancer risk, though the underlying biological mechanisms remain unclear. Research has shown that shorter LTL

[1]Oncology Department, Affiliated Zhongshan Hospital of Dalian University, No.6 Jiefang Street, Zhongshan District, Dalian 116001, Liaoning, PR China. [2]Department of Clinical Laboratory, Shandong Cancer Hospital and Institute, Shandong First Medical University, Shandong Academy of Medical Sciences, Jinan, Shandong, PR China. [3]Department of Pathology, Harbin Medical University, Harbin, Heilongjiang Province, PR China. [4]Shandong Provincial Key Laboratory of Precision Oncology, Shandong Cancer Hospital and Institute, Shandong First Medical University, Shandong Academy of Medical Sciences, Jinan, Shandong, PR China. [5]Shandong Cancer Hospital and Institute, Shandong First Medical University, Shandong Academy of Medical Sciences, 440 Ji-Yan Road, Jinan 250117, Shandong Province, PR China. ✉email: wangruoyu@dlu.edu.cn; xgsong@sdfmu.edu.cn

is a risk factor for certain cancers and poor prognosis. For example, LTL in patients with renal cell carcinoma, head and neck cancer, or bladder cancer are significantly shorter compared to controls[7,10–13]. Additionally, large cohort studies and randomization studies using genetic predictions of LTL have found that longer LTL is associated with an increased risk of several types of cancer[14–17].

The relationship between telomere length and NSCLC is still not fully understood. Some studies suggest that shorter telomeres may be associated with poor prognosis in lung cancer[18–20]. In 2019, Kachuri et al. analyzed two independent study populations and found that shorter LTL could be a marker for poor prognosis in NSCLC. Shorter LTL measured within five years of diagnosis was significantly associated with an increased risk of 5-year mortality in 767 NSCLC cases (HR = 1.52; 95% CI, 1.18–1.95; qFDR < 0.05), indicating its potential diagnostic value. In another cohort, shorter LTL (≤ 10th percentile) detected after diagnosis was associated with increased mortality in lung adenocarcinoma patients (HR = 1.65; 95% CI, 1.04–2.64; qFDR = 0.08)[18]. A study by Li et al. demonstrated that, among 369 patients with advanced lung adenocarcinoma, those with shorter LTL had a significantly lower median overall survival (OS) compared to those with longer LTL (12.9 months vs. 17.8 months, $p = 1.2 \times 10^{-4}$)[19]. Additionally, shorter leukocyte relative telomere length was significantly associated with poor prognosis after gefitinib treatment (HR = 1.65, 95% CI = 1.28–2.12; $p = 8.8 \times 10^{-5}$), suggesting that LTL could be a potential marker for EGFR-TKI therapy. However, some studies on early-stage NSCLC have shown that longer LTL in women with adenocarcinoma is associated with an increased risk of recurrence after curative resection[21]. These findings highlight the conflicting results regarding the relationship between telomere length and lung cancer.

In this study, we aim to examin LTL at different time points and figure out its association with NSCLC progression, and to explore the potential of LTL as a prognostic biomarker for resectable NSCLC. By measuring LTL in healthy controls, as well as pre- and post-operation resectable NSCLC patients, we assessed the distribution of LTL across different stages, the changes in LTL before and after surgery, and their impact on prognosis. Our findings indicate that, compared to healthy controls, lung cancer patients have significantly shorter telomeres, even in early-stage lung cancer, with a close correlation to cancer staging. LTL increases after surgery, and patients with longer post-operation telomere lengths have better prognosis. In conclusion, LTL has the potential to be an excellent prognostic biomarker for resectable NSCLC.

Materials and methods

Patients and clinical samples

The tumors were histologically classified and staged according to the 8th AJCC/UICC staging system. None of the enrolled patients were treated with chemotherapy, radiotherapy, immunotherapy or any other anti-tumor therapy before the specimen collection. The Po-LTL was assessed at the 3-month follow-up after the surgery, and the LTL change represented the absolute change in LTL between from pre-operation to post-operation samples, calculated as Po-LTL minus Pre-LTL. All healthy donors were healthy without signs or symptoms of active disease. The patients were followed up by telephone or by clinical visits, and the review of clinical and pathological data was provided by the electronic medical record.

Leukocyte telomere length (LTL) assessment

We determined the ratio of telomere repeat copy number (T) to single copy gene number (S) as a measure of relative telomere length by qPCR. The expression of gene copy number was determined on the Light-Cycler 480 qPCR system (Roche Diagnostics) using the SYBR Green Premix Pro Taq HS qPCR Kit (Accurate Biotechnology) following the manufacturer's instructions. The average LTL is calculated by the following formula: mean LTL = $\lg 2^{Ct\ (36B4)-Ct\ (Telomere)}$;[18] Primers: Telomere-F: CGGTTGTTTGGGTTTGGGTTTGGGTTTGGGTTTGGGTT; Telomere-R: GGCTTGCCTTACCCTTACCCTTACCCTTACCCTTACCCT; 36B4-F: CAGCAAGTGGGAAG GTGTAATCC; 36B4-R: CCCATTCTATCATCAACGGGTACAA.

Circulating TERT assessment

Blood samples were processed to obtain serum by centrifuging at 3000 g for 10 minutes. The levels of circulating TERT (telomerase reverse transcriptase) were measured using ELISA kits from Elabscience following the manufacturer's protocol. In summary, a 96-well plate was initially coated with an anti-human TERT antibody. Subsequently, 100 µl of the serum sample was introduced into the designated wells and incubated at 37℃ for 90 minutes. This was followed by incubation at the same temperature for 60 minutes with a biotinylated antibody and an additional 30-minute incubation with HRP-conjugated streptavidin. After washing the wells, a 3,3',5,5'-Tetramethylbenzidine (TMB) substrate solution was added and the reaction was allowed to proceed in the dark. Finally, the assay results were measured using the SpectraMax i3x Multi-Mode Microplate Reader (Molecular Devices).

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 22.0, the GraphPad Prism version 9.0.0 and R 4.4.2 for Windows. The data were assessed for normal distribution with the Kolmogorov–Smirnov Test. The t test is used when normality is not rejected; otherwise, the Mann-Whitney test was applied. One-way ANOVA or Kruskal–Wallis test was used for data analysis comparing more than two groups. Receiver operating characteristic (ROC) curves were used to assess sensitivity and specificity, and the area under the ROC curve was used as the performance metric. Kaplan-Meier analysis and univariate and multivariate Cox Proportional Hazard regressions were used to analyze DFS and OS, which were grouped according to according to the median of LTL level. All tests were two-sided, and p value < 0.05 was considered statistically significant.

Results

Study population

The flow diagram of the enrolled patients was presented in Fig. 1A total of 76 NSCLC patients were recruited between 1/01/2017 and 1/31/2019, and 69 patients were eligible for study participation for the resectable NSCLC after screening. Healthy donors' subjects were recruited as controls. For the study cohort included 25 Stage I, 16 Stage II, 21 Stage III, and 5 Stage IV NSCLC patients, the demographic information was listed in Table 1: age,

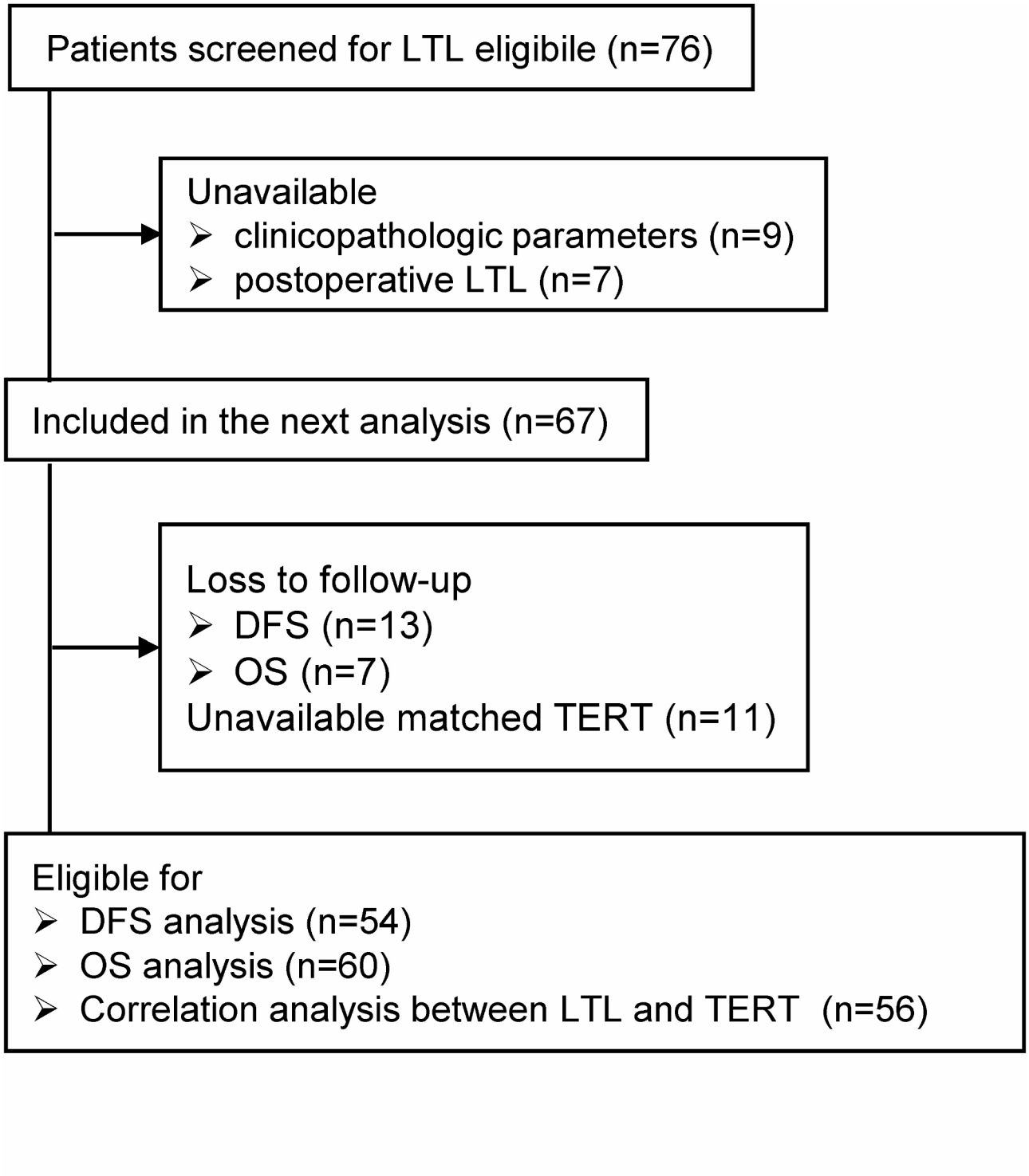

Fig. 1. Flow diagram of the enrolled patients. A total of 76 NSCLC patients were recruited between 9/01/2017 and 12/31/2018, and 67 patients were eligible for study participation after screening.

Parameter	Sample (*n*)	LTL median (IQR)	*p*-value
Age (years)			
≥61	34	2.110 (1.638 to 2.320)	0.4264
<61	33	2.020 (1.185 to 2.275)	
Not available	9		
Gender			
Male	43	2.040 (1.270 to 2.220)	0.6565
Female	24	2.210 (1.198 to 2.333)	
Not available	9		
Smoking			
Yes	30	2.035 (1.220 to 2.320)	0.9975
No	37	2.100 (1.315 to 2.305)	
Not available	9		
Histology			
AC	38	1.985 (1.178 to 2.303)	0.5008
SCC	21	2.190 (1.515 to 2.350)	
Others	8	2.135 (1.938 to 2.293)	
Not available	9		
T stage			
T1	24	2.145 (1.655 to 2.340)	0.3372
T2	34	2.005 (1.178 to 2.318)	
T3	5	2.040 (1.510 to 2.475)	
T4	4	1.490 (1.078 to 2.105)	
Not available	9		
LN metastasis			
N0	35	2.210 (1.960 to 2.370)	**0.0028***
N1	11	1.990 (1.380 to 2.210)	
N2	21	1.760 (1.140 to 2.125)	
Not available	9		
Distant metastasis			
M0	62	2.085 (1.515 to 2.318)	**0.0030***
M1	5	1.180 (0.640 to 1.490)	
Not available	9		
TNM stage			
I	25	2.220 (1.965 to 2.370)	**0.0008***
II	16	2.135 (1.920 to 2.308)	
III	21	1.880 (1.145 to 2.200)	
IV	5	1.180 (0.640 to 1.490)	
Not available	9		

Table 1. LTL related to the clinicopathologic parameters of NSCLC patients. *$p < 0.05$.

gender, behavioral factors, pathological type and disease stage. As shown in Table 1, LTL levels were positively correlate with the LN metastasis, distant metastasis and TNM stages in NSCLC patients.

Differential LTL in the resectable NSCLC

First, we analyzed the LTL in 76 patients and 80 healthy controls. As shown in Fig. 2A, LTL levels were significantly shorter in NSCLC patients compared to healthy controls, and this difference persisted even in stage I NSCLC (Fig. 2B) and early-stage (Fig. S1A). As cancer progresses, a clear trend toward a gradual decreasing of LTL was observed, particularly between stage I and stages II-IV (Fig. S1B), as well as between stages I/II and III/IV (Fig. 2C). However, no statistically significant difference was found between stage I and II (Fig. S1C). No significant differences in LTL were observed across stages T1 to T4, additionally, a reduction of LTL in stage T2 was noted (Fig. 2D). Analysis of LTL across different N and M stages revealed a gradual decrease in LTL as the cancer stage advanced (Fig. 2E-F).

Dynamic changes of LTL in NSCLC patients

We detected the differences between Pre- and Po-LTL paired. The Po-LTL levels were significantly elevated (Fig. 3A), but no significant differences were observed between paired Pre- and Po-LTL levels in stage I and early-stage NSCLC patients (I + II) (Fig. S1D-E). In contrast, in advanced-stage patients (III + IV), LTL levels showed a significant increase (Fig. 3B). Interestingly, Po-LTL levels in early-stage (I + II) were still significantly

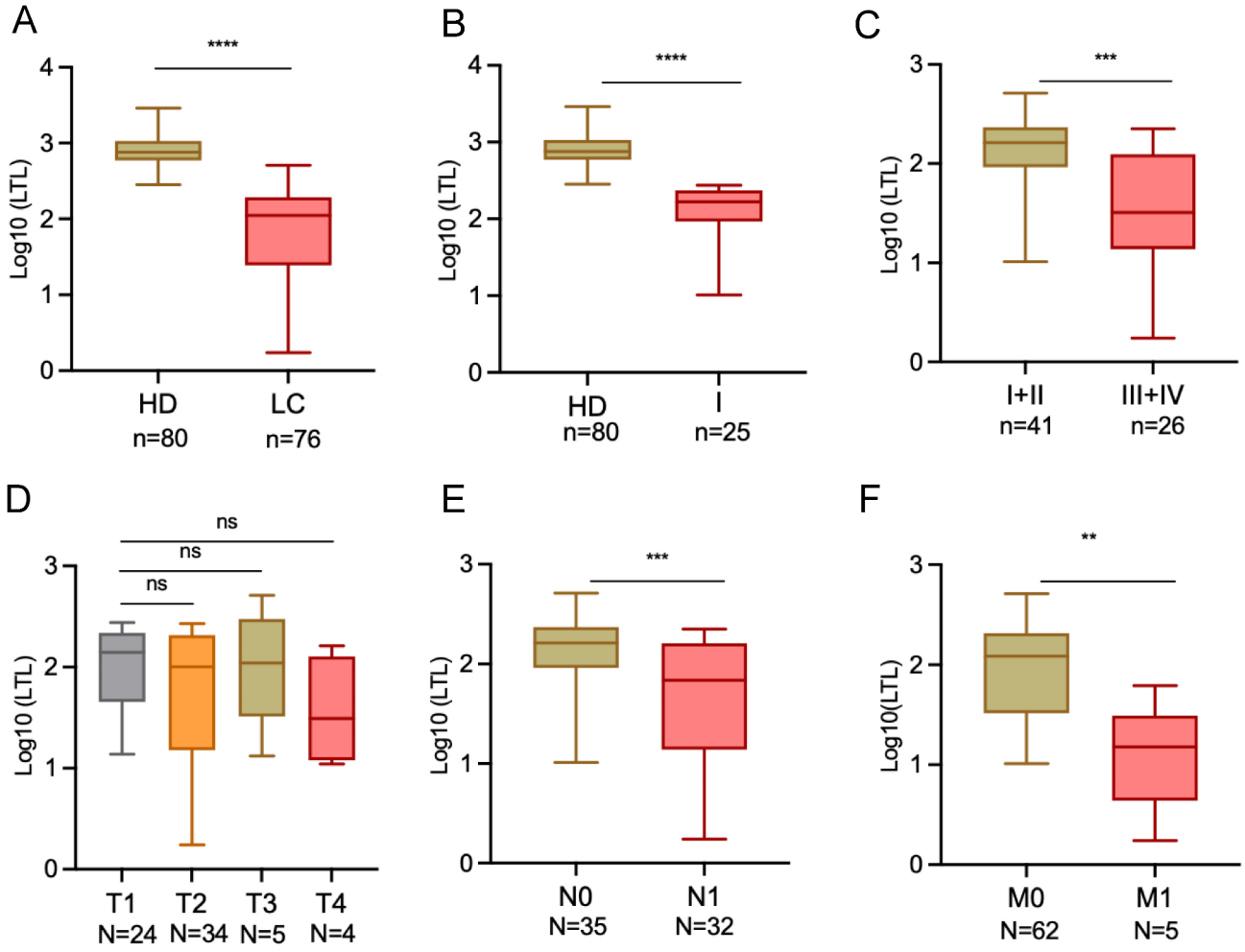

Fig. 2. Distribution of LTL in resectable non-small cell lung cancer. The LTL was analyzed between NSCLC patients and healthy controls (**A**), between Stage I NSCLC and the healthy (**B**), between Stage I-II and the Stage III-IV NSCLC (**C**), between different T, N and M stage NSCLC(D-F).

lower than the HD cohort (Fig. 3C). Then, we evaluated dynamic changes of LTL in all patients and found that Po-LTL was significantly elevated than Pre-LTL, however, they did not reach the levels observed in healthy controls (Fig. S1F).

Next, we examined the relationship between Po-LTL and clinicopathologic parameters (Table S1). No significant correlation was found between Po-LTL and these parameters, including gender, age, smoking, pathology, lymph node metastasis, distance metastasis and TNM stage. Finally, we analyzed the changes in LTL within the initial 3 months following surgical intervention, which might be indicative of the surgery therapy on telomere dynamics. The LTL change was found to correlate with distant metastasis and TNM stage. Specifically, a greater LTL change was observed in patients with more advanced cancer stages (Table S2).

Post-LTL predicts the prognosis of resectable NSCLC

The association between LTL levels and survival outcomes was analyzed in all enrolled NSCLC patients, who were divided into long and short groups based on the median LTL value. The OS was significantly longer in the long Po-LTL group compared to the short LTL group ($p = 0.0024$, Fig. 4A). However, no significant effect of Po-LTL on DFS was observed (Fig. 4B). Next, we examined the impact of Pre-LTL and LTL change on survival outcomes. No significant correlations were found between Pre-LTL or LTL change and either DFS or OS (Fig. S2 A-D). Additionally, the prognostic value of Po-LTL and clinicopathological factors for OS (Table 2) and DFS (Table 3) was evaluated using both univariate and multivariate regression analyses. Po-LTL was identified as an independent prognostic factor for OS in both univariate ($p = 0.006$, Fig. 4C) and multivariate ($p = 0.003$, Fig. 4D) analyses, but did not show significance for DFS in either analysis (Table 3).

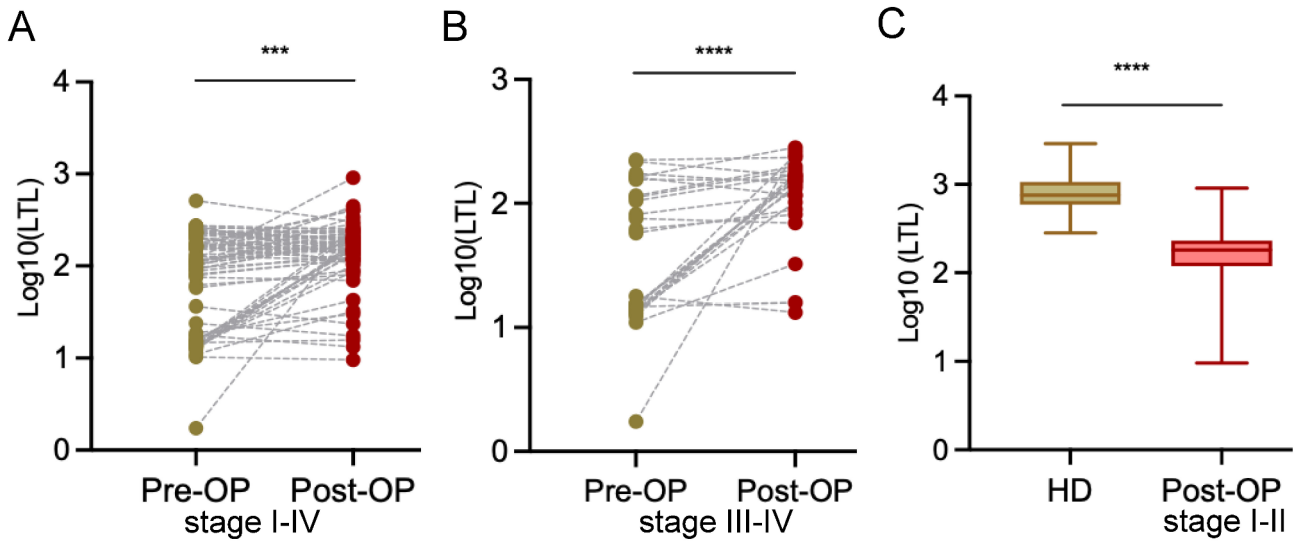

Figure 3

Fig. 3. Dynamic changes of LTL in NSCLC patients. Comparison of LTL between paired pre-OP and post-OP in all NSCLC (**A**), comparison of LTL between paired pre-OP and post-OP in Stage III-IV NSCLC (**B**), comparison of LTL between healthy controls and post-OP in Stage I-II NSCLC (**C**).

Post-operation LTL combined with TNM stage as a prognostic marker for resectable NSCLC OS and DFS

We found that Po-LTL was an independent prognostic factor for OS. Further, we combined the critical prognostic factor, TNM stage, with Po-LTL to analyze its predictive capability for the prognosis of resectable NSCLC patients. The results indicated that the long Po-LTL + stage I/II group had the best prognosis, while the short Po-LTL + stage III/IV group had the poorest prognosis for both OS ($p < 0.001$, Fig. 5A) and DFS ($p < 0.001$, Fig. 5C). The area under the curve (AUC) analysis demonstrated that the combination of Po-LTL and TNM stage provided a good prediction for 5-year OS (Fig. 5B), with an AUC of 0.680, and for DFS (Fig. 5D), with an AUC of 0.652, both of which were higher than the predictive power of TNM stage alone. The restricted mean survival time (RMST) of 5-year survival was compared between short and long LTL in OS and DFS. The RMST of OS at 5 years was 4.67 years (95% CI: 4.27–5.08) in the long LTL group and 3.42 years (95% CI: 2.82–4.02) in the short LTL group. The difference in RMST between the long and short LTL groups was 1.26 years (95% CI: 0.53–1.98, $p = 0.001$), indicating a statistically significant survival advantage for the long LTL group (Fig. S2E). The RMST of DFS at 5 years was 3.55 years (95% CI: 2.88–4.22) in the long LTL group and 2.90 years (95% CI: 2.15–3.65) in the short LTL group. While the RMST was numerically higher in the long LTL group, the difference of 0.65 years (95% CI: -0.36-1.66, $p = 0.206$) was not statistically significant (Fig. S2F).

The correlation between LTL and circulation TERT

TERT serves as the catalytic component of telomerase, essential for maintaining telomere length and enabling cellular self-renewal[5]. This function is particularly crucial in cancer cells, which evade senescence by preserving telomere length primarily through telomerase activation[22]. In the present study, we measured the levels of LTL and circulating TERT in patients with resectable NSCLC before and after surgery to explore their correlation (Fig. S3). Figure S3A displays the overall distribution of Pre-LTL across different disease stages, including healthy donors and post-operative samples, providing a broad context for comparison with circulating TERT levels. Circulating TERT levels significantly increased as NSCLC progressed and continued to a decrease in the post-operation group (Fig. S3B). Healthy Donors (HD) had a median of 0.145 with an IQR of 0.077 to 0.271; Stage I had a median of 0.651 with an IQR of 0.455 to 0.886; Stage II had a median of 0.743 with an IQR of 0.511 to 1.259; Stage III had a median of 0.772 with an IQR of 0.501 to 1.319; Stage IV had a median of 1.609 with an IQR of 0.750 to 1.857; and the Post-Operation group had a median of 1.363 with an IQR of 0.817 to 2.305 (TERT: ng/ml, Fig. S3B). No direct correlation was observed between LTL and TERT levels either before or after surgery (Fig. S3C-D). Further investigation is needed to fully elucidate the interplay between LTL and TERT in NSCLC and explore the complex dynamics of telomere length and telomerase activity in this disease.

Discussion

Telomere length is a potential biomarker for the prediction of prognosis in resectable NSCLC patients. Our study, which assessed LTL in a small cohort of NSCLC patients, reveals a significant relationship between LTL

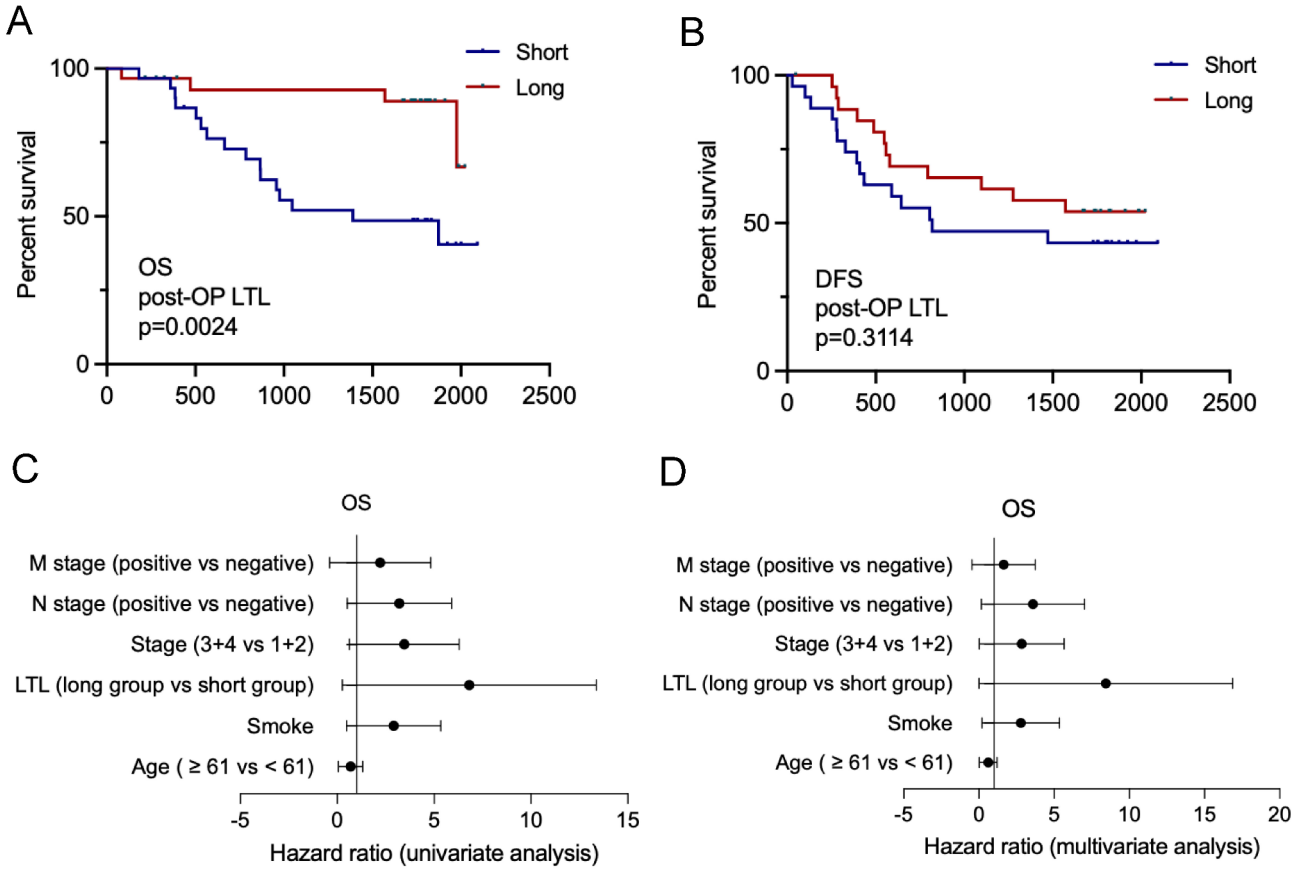

Figure 4

Fig. 4. Po-LTL predicts the prognosis of resectable NSCLC. Kaplan-Meier OS (**A**) and DFS (**B**) analysis with Po-LTL using log-rank test. Univariate (**C**) and multivariate analysis of NSCLC patients based on COX regression mode.

Characteristics	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age (≥61vs < 61)	0.503 (0.182–1.390)	0.185	0.427 (0.143–1.277)	0.128
Smoke	2.239 (0.892–5.619)	0.086	1.986 (0.697–5.663)	0.199
LTL (high group vs. low group)	4.710 (1.566–14.163)	**0.006***	5.629 (1.769–17.916)	**0.003***
Stage (3 + 4 vs. 1 + 2)	2.690 (1.096–6.602)	**0.031***	1.909 (0.606–6.013)	0.270
N stage (positive vs. negative)	2.459 (0.976–6.196)	0.056	2.496 (0.838–7.433)	0.100
M stage (positive vs. negative)	1.190 (0.273–5.181)	0.816	0.742 (0.136–4.048)	0.730

Table 2. The univariate and multivariate analysis of post-operative LTL and clinicopathologic variables associated with OS in the resectable NSCLC patients.

and the stages of NSCLC. First, we observed a notably shorter LTL in patients compared to healthy donors. Specifically, healthy individuals exhibited significantly longer LTL compared to patients with stage I–II NSCLC. These findings suggest that LTL could serve as an early diagnostic marker for NSCLC. Furthermore, we report for the dynamic changes in LTL pre- and post- operation and their relationship with patient prognosis. In our study, Po-LTL levels were significantly higher than pre-LTL levels in patients with stage III–IV disease. While not statistically significant, we did observe a trend towards LTL changes in Stages I and II. When we categorized resectable NSCLC patients based on LTL, we found that Po-LTL was significantly correlated with OS.

Several studies support our findings. In 2023, Belić et al. reported a significant shortening of LTL in NSCLC patients compared to healthy controls ($P < 0.001$), with stage IV patients showing significantly shorter telomeres

Characteristics	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age (≥61vs < 61)	1.156 (0.543–2.460)	0.707	0.981 (0.432–2.225)	0.963
Smoke	1.659 (0.775–3.552)	0.192	1.545 (0.636–3.754)	0.336
LTL (high group vs. low group)	0.778 (0.364–1.663)	0.517	0.813 (0.365–1.810)	0.612
Stage (3 + 4 vs. 1 + 2)	2.909 (1.352–6.256)	**0.006***	1.969 (0.669–5.799)	0.219
N stage (positive vs. negative)	2.741 (1.246–6.030)	**0.012***	2.011 (0.770–5.256)	0.154
M stage (positive vs. negative)	1.286 (0.386–4.287)	0.682	0.704 (0.175–3.823)	0.620

Table 3. The univariate and multivariate analysis of post-operative LTL and clinicopathologic variables associated with DFS in in the resectable NSCLC patients. $^{*}p < 0.05$.

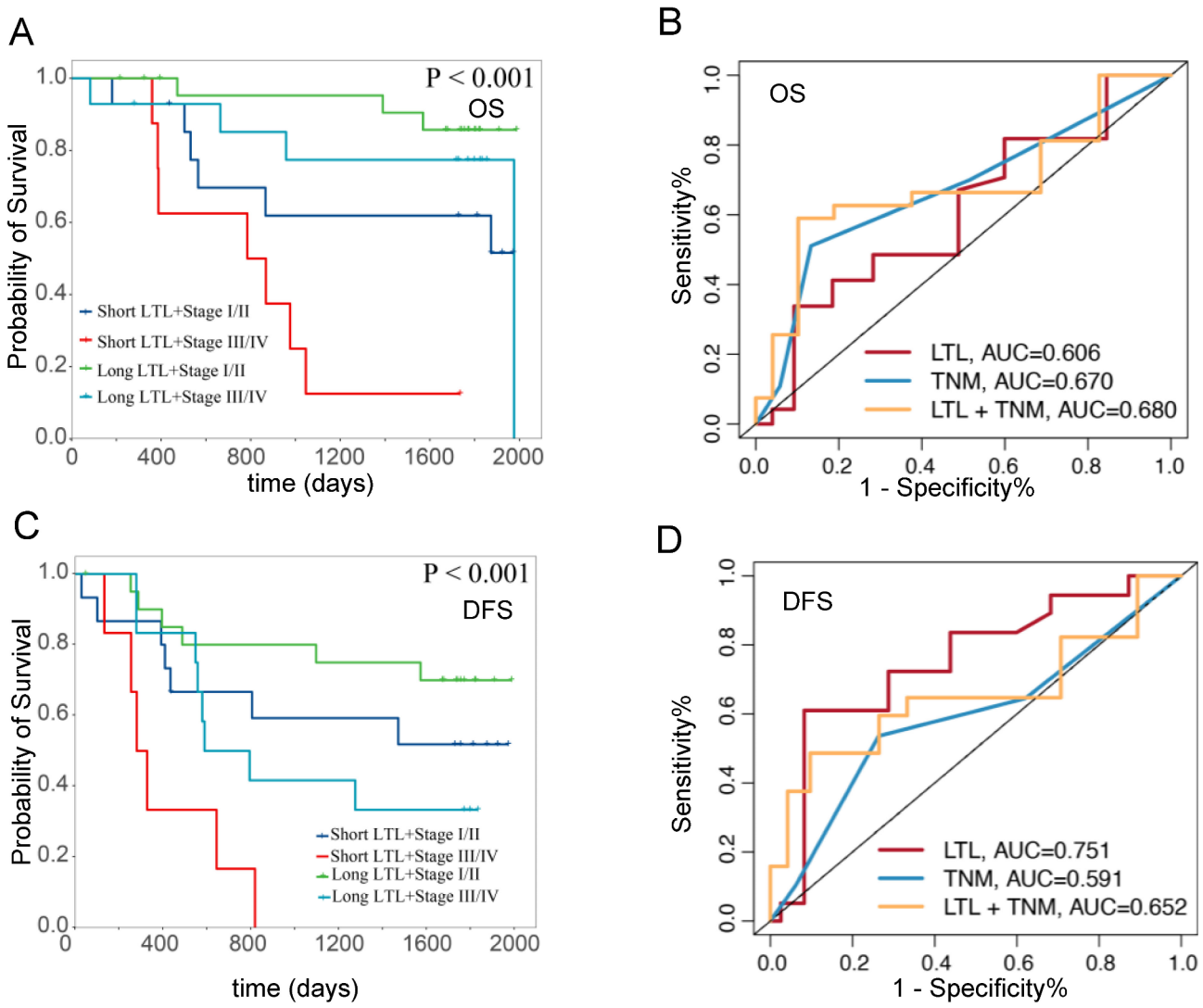

Fig. 5. Post-LTL combined with TNM staging predicts the prognosis of resectable NSCLC. LTL combined with TNM staging analysis of OS (**A**) and DFS (**C**) in resectable NSCLC. ROC curves of 5-year OS (**B**) and DFS (**D**) in resectable NSCLC.

than those with stage I-III disease ($P = 0.014$)[20]. Furthermore, prospective studies have shown that shorter pre-diagnostic telomere length is significantly associated with an increased 5-year mortality risk in lung cancer patients[18]. However, some studies have reported longer LTL levels in NSCLC patients compared to healthy controls[23], and a prospective study by Kim et al. found that longer LTL were associated with a higher risk of recurrence in patients with early-stage after curative resection[21]. These conflicting results may be attributed to factors such as differences in disease progression, treatment regimens, ethnic variations, and the methods used to measure telomere length.

Interestingly, when we analyzed the dynamic changes in telomere length three months post-surgery, we observed a certain degree of Po-LTL increase. This change was significantly correlated with distant metastasis and TNM staging, independent of factors such as gender, age, smoking status, pathology, T staging, and lymph node metastasis. Similar conclusions were reached in studies on breast cancer and colorectal cancer[24,25]. The LTL is longest in healthy individuals but progressively shortens with advancing pathological stages, likely due to cumulative tumor burden and systemic stress. Notably, Stage III–IV NSCLC patients with the shortest Pre-LTL, demonstrated the most pronounced LTL recovery after resection (Fig. 3B), suggesting that surgical removal of high-burden tumors alleviates telomere attrition. However, while dynamic LTL changes were more prominent in advanced stages which were closely associated with metastasis and TNM stage (Table S2), post-operative LTL itself—rather than its dynamic change—emerged as a stronger prognostic biomarker for survival outcomes (Fig. 4A; Table 2), potentially reflecting residual tumor biology or baseline telomere integrity.

Although TERT is pivotal in regulating telomere length, circulating TERT may not play a role in maintaining leukocyte telomere length. This is because circulating TERT exists as a cell-free protein in the bloodstream, originating from cancer cells, normal tissue cells, and blood cells. Additionally, multiple other mechanisms influence TERT expression and telomerase activation. Inflammation and differences in telomerase activity within leukocytes could be influencing the relationship between LTL and circulating TERT. Chronic inflammation, a hallmark of NSCLC progression, can induce telomere shortening through increased cellular turnover and oxidative stress[26,27]. Furthermore, oxidative stress, a consequence of NSCLC-related metabolic changes, and epigenetic modifications affecting TERT expression could be influencing the relationship between LTL and circulating TERT. Increased oxidative stress can accelerate telomere shortening, potentially masking any direct relationship with circulating TERT level[28,29]. Therefore, we propose that circulating TERT likely has minimal direct association with LTL, and both factors may independently serve as prognostic indicators for NSCLC.

Although our findings highlight the clinical relevance of LTL in optimizing postoperative management, several limitations should be taken into consideration. First, the sample size was relatively small, particularly for stage IV NSCLC patients ($n = 5$, exclusively oligometastatic cases), which limits the generalizability of the findings and robust conclusions about LTL dynamics in advanced disease. Second, the study only included patients who underwent surgical resection, thereby these results may not be applicable to the broader NSCLC patient population who receive chemotherapy, radiotherapy, or immunotherapy. Finally, LTL measurements were limited to pre- and post-operative time points (3 months after surgery), and longer-term LTL changes and their impact on prognosis were not assessed. To address this gap, future investigations should prioritize expanding stage IV cohorts, particularly those undergoing multimodal therapies, to elucidate longitudinal LTL changes and their prognostic implications in metastatic NSCLC.

In conclusion, this study systematically investigates LTL dynamics and its prognostic value in resectable NSCLC. We demonstrated that NSCLC patients have significantly shorter LTL than healthy controls, with LTL inversely correlated to disease stage. Pos-LTL levels were associated with improved OS, emerging as an independent prognostic marker. Although the underlying mechanisms of LTL in tumorigenesis and progression remain incompletely understood, our findings suggest that LTL holds significant promise potential for post-operative NSCLC management.

Data availability

The data sets used and/or analyzed during the present study are available from the corresponding author on request: xgsong@sdfmu.edu.cn.

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Author contributions

Investigation, Methodology, Validation: Guanxuan Chen and Shiwen Wang; Formal analysis and investigation: Guanxuan Chen and Qianru Zhang; Data curation: Junyan Liu and Wanqi Zhu; Writing—original draft preparation, Guanxuan Chen; Writing—review, revision and editing, Xingguo Song and Ruoyu Wang; Supervision: Xingguo Song and Ruoyu Wang; Funding acquisition: Xingguo Song. All authors have read and agreed to the published version of the manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Shandong Cancer Hospital Affiliated to Shandong First Medical University and Shandong Academy of Medical Sciences with full respect to the 1964 Helsinki Declaration.

Informed consent

All detections in the current study were carried out using the remaining sample after completing clinical inspection, and the requirement for informed consent was waived, which had been approved by the Ethics Committee of Shandong Cancer Hospital Affiliated to Shandong First Medical University and Shandong Academy of Medical Sciences.

Additional information

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Correspondence and requests for materials should be addressed to R.W. or X.S.