Cellular and Molecular Biology
E-ISSN : 1165-158X / P-ISSN : 0145-5680
www.cellmolbiol.org

The relationship between the expression of lncRNA MALAT1 and clinical features and prognosis in bladder cancer: A meta-analysis

Yi Su[1], Hong Chen[2], Lifeng Yao[1], Hao Dai[1], Houxian Liu[1*]

[1] Department of Urology, Zhejiang Cancer Hospital Ningbo Branch (Ningbo Fenghua District People's Hospital), Ningbo 315500, China
[2] Operating Room, Zhejiang Cancer Hospital Ningbo Branch (Ningbo Fenghua District People's Hospital), Ningbo 315500, China

ARTICLE INFO

Meta-analysis

Article history:
Received: July 02, 2023
Accepted: September 24, 2023
Published: December 20, 2023

Keywords:

LncRNA MALAT1; Bladder cancer; Prognosis; Meta-analysis

ABSTRACT

The objective of this meta-analysis is to evaluate the association between LncRNA MALAT1 and the clinicopathological characteristics and prognosis in patients with bladder cancer. Related studies were searched from Pubmed, Embase, Cochrane Library, CNKI and Web of Science up to Sep 1, 2021. Basic characteristic and prognostic data were extracted from the included studies. We synthesized and compared primary outcomes such as overall survival. Based on the cut-off value, sample size, and follow-up time, subgroup analysis was conducted. We calculated the combined hazard ratio (HR), odds ratio (OR), and 95% confidence interval (CI) to assess the relationship between LncRNA MALAT1 and prognosis clinicopathological features of bladder cancer patients. Seven studies with 822 patients were included in this meta-analysis. The results showed that the high lncRNA MALAT1 was significantly related to poor overall survival (HR = 2.34, 95% CI:1.61-3.38; P<0.001) in bladder cancer patients. Furthermore, a high level of LNCRNA MALAT1 is associated with lymph node metastasis (LNM) (OR = 1.82, 95% CI 1.32-2.52, P <0.001) in bladder cancer. The results of sensitivity analysis showed the stabilization and reliability of results in this Meta-analysis. In conclusion, elevated LncRNA MALAT1 is associated with a poor prognosis and a higher risk of LNM in patients with bladder cancer. LncRNA MALAT1 could be identified as a biomarker with a potential prognostic value in bladder cancer.

Doi: http://dx.doi.org/10.14715/cmb/2023.69.14.27

Introduction

Bladder cancer is a common malignant tumor of the genitourinary system, ranking 11th in incidence among malignant tumors (1). Worldwide, about 150,000 people die from bladder cancer each year (2). The occurrence of bladder cancer is multicentric in nature and has a high rate of recurrence after surgery, requiring frequent review and long-term follow-up of patients, which is a great burden for their families and society (3, 4). Therefore, it is of great significance to explore the pathological factors affecting the invasion and metastasis of bladder cancer.

LncRNAs are a class of RNA molecules greater than 200 nt in length that do not encode proteins (5) and can regulate gene expression at different levels, including chromatin modification, transcriptional level and post-transcriptional level, and are closely related to many human diseases, especially tumors (6, 7). Metastasis-associated lung adenocarcinoma transcript 1 (LncRNA MALAT1), has received increasing attention as a highly conserved LncRNA associated with many diseases, especially cancer (8). LncRNA MALAT1 is up-regulated in several tumor types and is associated with biological properties such as tumor cell proliferation, migration, invasion and apoptosis (9). Knockdown of the LncRNA MALAT1 gene in bladder cancer cells inhibits cell proliferation, invasion, and tumor formation (10). Ren et al. (11) showed that LncRNA MALAT1 was up-regulated in human bladder cancer tissues and cell lines, and high LncRNA MALAT1 expression correlated with high Gleason score, PSA, and tumor stage. In AR-negative DU 145 and PC 3 cells, knockout of lncRNA MALAT1 inhibited cell proliferation and migration, and promoted cell apoptosis (12). All of the above studies suggest that MALAT1 plays a key role in bladder cancer progression, reflecting its potential role as a target for tumor-targeted therapy.

At present, the related research results of lncRNA MALAT1 prediction of bladder cancer patients are inconsistent, and the sample size is small. Considering the heterogeneity and potential value of LncRNA MALAT1 detection, this study aims to explore the prognostic value of LncRNA MALAT1 in patients with bladder cancer.

Materials and Methods

Search Strategy

The search was conducted in Pubmed, Embase, Cochrane Library, CNKI (China National Knowledge Infrastructure) and Web of Science from inception to Sep 1, 2021. Search published studies on the relationship between LncRNA MALAT1 and the prognosis of bladder cancer. And the studies are published in English and Chinese. The search terms were "LncRNA MALAT1", "MALAT1", "bladder cancer", "bladder tumor", "bladder neoplasm", "survival", "outcome" "prognosis" and "recurrence". The following keywords for the online search in these databases were included: ("LncRNA MALAT1" OR "MALAT1") AND ("bladder carcinoma" OR "bladder can-

* Corresponding author. Email: houxian858@163.com

cer" OR "bladder tumor" OR "bladder neoplasm") AND ("prognosis" OR "prognostic" OR "survival" OR "outcome" OR "recurrence"). Two researchers independently searched the literature and finally cross-checked to reach an agreement.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (i) The subjects were bladder cancer patients. (ii) studies with participants divided into two groups of high and low lncRNA MALAT1 level; (iii) articles that explored the association between LncRNA MALAT1 expression and of overall survival (OS) of bladder cancer; (iv) studies with the inclusion of sufficient data such as hazard ratio (HR) and corresponding 95% confidence interval (CI) for the computation of pooled HR and 95% CI.

Exclusion criteria were as follows: (i) reviews, letters, case reports, and non-human subject research; (ii) articles with missing and ambiguous data; (iii) Newcastle-Ottawa Scale (NOS) score less than six. (iv) the follow up less than 50 months.

Quality Assessment

The quality of the included study was evaluated according to the NOS (13). The study was scored from object selection, comparability, outcome and exposure with a maximum score of nine points. A score of ≥6 points can be regarded as high-quality literature. If there is any disagreement, two researchers would discuss it together, and a third researcher would be invited to participate in the discussion and achieve the consistency of the result.

Data Extraction

Two researchers extracted data and evaluated study quality independently. The study was strictly screened according to inclusion and exclusion criteria. We extracted the following information from the original literature: (1) basic characteristics: First author, country, year, sample size, pathology, follow-up time; (2) the outcome of clinicopathologic parameters: Number of bladder cancer cases in high and low LNCRNA MALAT1 level group based on age, lymph node metastasis (LNM), Tumor node metastasis (TNM) stage, and tumor size; (3) the outcome of prognosis: HR and its 95%CI. The basic research information to be collected directly includes author, country and publication time, sample size, cut-of-value and original data (hazards ratio and 95% confidence interval). If only Kaplan-Meier survival curve data were available for eligible studies, data such as HR and 95% CI were extracted from the graphs using the Enguage digitizer software (version 4.1) (14).

Statistical Analysis

For the meta-analysis, the pooled HR and OR were conducted by software programs Review Manager 5.3 software (The Cochrane Collaboration, Copenhagen, Denmark) and Software for Statistics and Data Science (STATA, version 12.0; College Station, TX, USA). If the eligible study only provides Kaplan-Meier survival curve data, the Enguage digitizer software was used to extract survival information such as HR and 95% CI from the graph. Heterogeneity among studies was assessed according to the size of statistic I^2. If $I^2 \geq 50\%$, or $P \leq 0.05$, there was significant heterogeneity among the included studies, and then a random-effects model was used. If $I^2 < 50\%$, or $P \leq 0.05$, there was no significant heterogeneity existed among the pooled data, and a fixed-effects model will be selected. When there was significant heterogeneity, we performed subgroup analysis to explore the source of heterogeneity. Subgroup analyses of primary outcomes were performed according to cut-off value (mean vs. median), follow-up time (≥ 80 vs. < 80 mouths) and sample size (n ≥ 120 vs. < 120). Pooled odds ratio (OR) and 95% CI were used to evaluate the relationship between LNCRNA MALAT1 and LNM, TNM stage, and distant metastasis. Publication bias was assessed by examining the funnel plot of each outcome. Then Egger's test was used to further examine the results, in which the natural logarithmic relative risk was plotted with SE. To evaluate the effect of individual studies on the estimated hazard ratio, sensitivity analysis was performed to re-evaluate the pooled hazard ratio by omitting one study at a time. $P < 0.05$ was considered statistically significant.

Results

Characteristics of Eligible Studies

A flow diagram of the literature selection was performed for this study (Figure 1). A total of 112 literatures were retrieved according to the retrieval strategy, and 72 literatures were excluded from repeated publications, reviews, abstracts, case reports, and non-prognostic and non-malignant tumor-related literatures. After reading the full text, 8 articles without relevant indicators of survival outcome were excluded, and finally, 7 articles were included (15-21). The characteristics of the 7 included studies are summarized in Table 1. These included studies were published from 2014 to 2020 with the sample size ranging from 60 to 188. Multivariate analysis was adopted in 6 studies respectively (15-20). The follow-up months ranged from 60 to 90 months. NOS scores range from a low of 6 to a high of 8 (Table 2).

Association between LncRNA MALAT1 and Prognosis of Bladder Cancer Patients

A total of 7 studies with OS as the end-point was included, and a total of 822 patients explored the correlation between LncRNA MALAT1 level and OS in bladder cancer (15-21). Combined HR and 95% of OS compliance data were collected from the above-mentioned inclusion studies. Using the random-effects model (I^2 = 64%, P = 0.01), the result indicated that high level of LncRNA MALAT1 in bladder cancer patients was related to poor OS

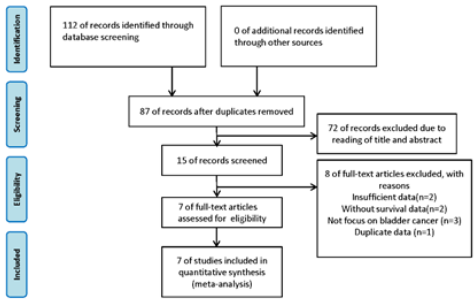

Figure 1. The flow diagram of this meta-analysis.

Table 1. Characteristics of studies in this meta-analysis.

Study	Year	Country	Cancer type	Total	Tumor stage	Cut of	MALAT1 expression				Survival analysis	Multivariate analysis	HR statistic	HR (95% CI)	Follow-up months	NOS score
							High expression	High with LNM	Low expression	Low with LNM						
Duan (15)	2016	China	BC	188	I–IV	Median	95	63	93	25	OS	rep	SC	0.613 (0.284–1.322)	80	8
Fan (16)	2014	China	BC	95	I–IV	Median	45	20	50	13	OS	rep	SC	2.99(1.73-5.16)	90	7
Li (17)	2017	China	BC	120	I–IV	Mean	64	21	56	7	OS	rep	SC	2.056(1.236-3.419)	60	7
Liang (18)	2021	China	BC	90	I–IV	Median	79	61	11	2	OS	rep	SC	3.278 (2.159-4.976)	60	8
Zhan (18)	2018	China	BC	60	I–IV	Mean	38	19	22	6	OS	rep	SC	3.627(1.483-8.872)	80	7
Zhang (20)	2016	China	BC	120	I–IV	Mean	62	22	58	6	OS	rep	SC	2.342(1.524-3.601)	60	8
Zhou (21)	2020	China	BC	149	I–IV	Mean	83	72	66	17	OS	NA	SC	3.317(1.325-8.313)	80	7

BC: bladder cancer; HR: hazard ratio; LNM: lymph node metastasis; NA: no report; OS: overall survival; Rep: report; RT-qPCR: real-time quantitative polymerase chain reaction; SC: survival curve; NOS: Newcastle-Ottawa scale.

Table 2. Study quality was assessed according to the Newcastle-Ottawa Scale.

study	Selection			comparability			outcome			total
	Adequacy of case definition	Representativeness of the cases	Selection of Controls	Definition of Controls	Ascertainment of exposure	Ascertainment of detection method	Ascertainment of cut-off	Assessment of outcome	Adequate follow up	
Duan 2016	1	1	1	1	1	0	1	1	1	8
Fan 2014	1	1	1	0	0	1	1	1	1	7
Li 2017	1	1	1	0	1	1	1	1	0	7
Liang 2021	1	1	1	1	1	1	1	1	0	8
Zhan 2018	1	1	1	0	1	1	0	1	1	7
Zhang 2016	1	1	1	1	1	1	1	1	0	8
Zhou 2020	1	1	1	1	1	1	0	1	0	7

(Pooled HR = 2.34, 95% CI:1.61-3.38; P<0.001) (Figure 2). The results showed that LncRNA MALAT1 was related to the OS of patients with bladder cancer, and the high level of LncRNA MALAT1 was an adverse factor for the prognosis of patients with bladder cancer.

Subgroup Analysis

These results confirmed that high expression of LncRNA MALAT1 in cancer tissues is a significant biomarker of the poor prognosis of patients with bladder cancer. As the moderate heterogeneity, we also analyzed the cut-off value, follow-up time and sample size by subgroup stratification. After stratification by sample size, we observed that lncRNA MALAT1 was a prognostic factor in the sample size (n < 120) (HR = 3.22, 95% CI: 2.36-4.40, P < 0.001) with no heterogeneity (I^2 = 0.0%, P > 0.1) (Figure 3A). For the cut-off value to divide the level of LncRNA MALAT1, we found that the predictive value was significant in the mean groups (HR = 2.44, 95% CI: 1.82-3.26, P < 0.001) with no heterogeneity (I^2 = 0.0%, P > 0.1) (Figure 3B). Subsequently, we also found that LncRNA MALAT1

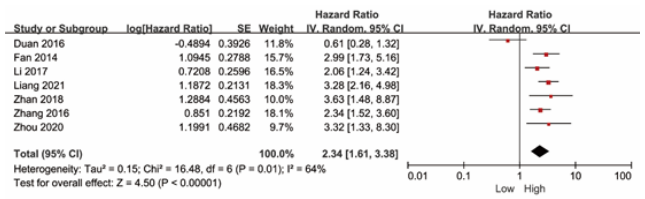

Figure 2. Meta-analysis of the pooled HRs and OS in bladder cancer with the expression level of LncRNA MALAT1.

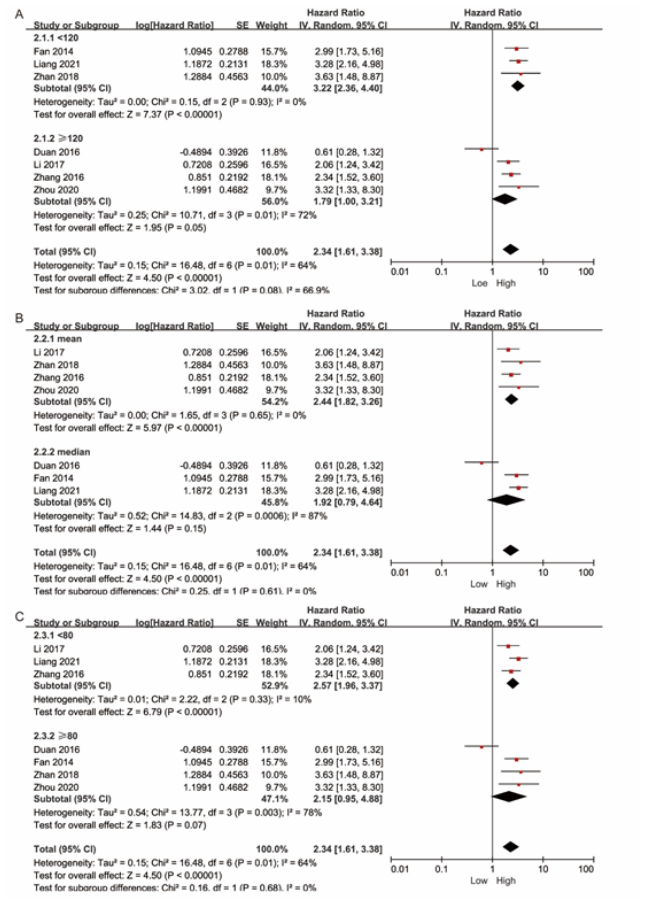

Figure 3. Subgroup analysis of hazard ratios for the association between LncRNA MALAT1 expression and overall survival. (A) sample size; (B)cut-off; (C) follow up time.

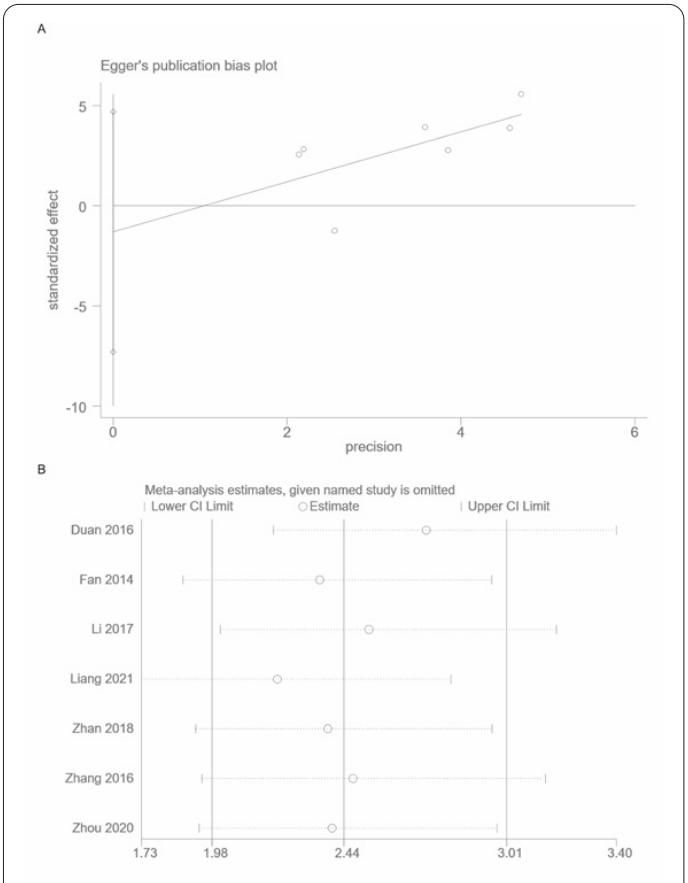

Figure 4. Risk of bias and sensitivity analysis of the meta-analysis. (A)Egger's test and (B) sensitivity analysis of poor HR for heterogeneity analysis.

could act as a prognostic factor in groups with follow-up time (< 80 mouths) (HR = 2.57, 95% CI: 1.96-3.37, P < 0.001) with low heterogeneity (I^2 = 10.0%, P > 0.1) (Figure 3C).

Risk of Bias and Sensitivity Analysis

The result of Egger' test (Figure 4A) indicated that there is no statistical significance in publication bias (P = 0.11). With regard to the studies of the relationship between LncRNA MALAT1 and OS in bladder cancer patients, after excluding all studies, no obvious changes of combined HR were found, which indicated that the results were relatively stable and reliable. (Figure 4B).

Association between LncRNA MALAT1 and clinicopathological features in bladder cancer patients

To analyze the association between LncRNA MALAT1 and clinicopathological characteristics in bladder cancer patients, we conducted the pooled results including age, lymph node metastasis (LNM), TNM stage, tumor size, and distant metastasis (Table 3). The results indicated that no significant association was detected between lncRNA MALAT1 expression and age (OR = 0.87, 95% CI:0.66-1.16, P = 0.34) (Figure 5A), gender (OR = 1.00, 95% CI:0.75-1.33, P = 0.99) (Figure 5B), TNM stage (OR = 1.74, 95% CI:0.89-3.40, P = 0.10) (Figure 5D) and tumor size (OR = 1.03, 95% CI:0.69-1.55, P = 0.87) (Figure 5E). Interestingly, high lncRNA MALAT1 was significantly correlated with LNM (OR = 3.49, 95% CI: 2.23–5.48, P<0.001) with low heterogeneity (I^2 = 5%, P = 0.38 (Figure 5C).

Table 3. Results of association between LncRNA MALAT1 and characteristics of patients with bladder cancer.

Stratified analysis	No. of studies	No. of patients	Pooled HR/OR (95% CI)	p-value	Heterogeneity		
					I^2, %	p-value	Model
OS							
Overall	7	822	2.34 (1.61, 3.38)	<0.001	64	0.01	Random effects
Clinicopathological features							
Age(≥60 vs. <60)	7	822	1.15 (0.87, 1.53)	0.33	0	0.71	Fixed effects
Gender(male vs. female)	7	822	1.0 (0.75, 1.33)	0.99	0	0.99	Fixed effects
LNM (Yes vs. No)	5	485	3.49 (2.23, 5.48)	<0.001	5	0.38	Fixed effects
TNM stage (III-IV vs. I-II)	5	485	1.74 (0.89, 3.40)	0.10	63	0.03	Random effects
Tumor size (≥3 cm vs. <3 cm)	4	425	1.03 (0.69, 1.55)	0.87	0	0.47	Fixed effects

CI: confidence interval; HR: hazard ratio; OR: odds ratio; LNM: lymph node metastasis; OS: overall survival; TNM: tumor node metastasis; vs: versus.

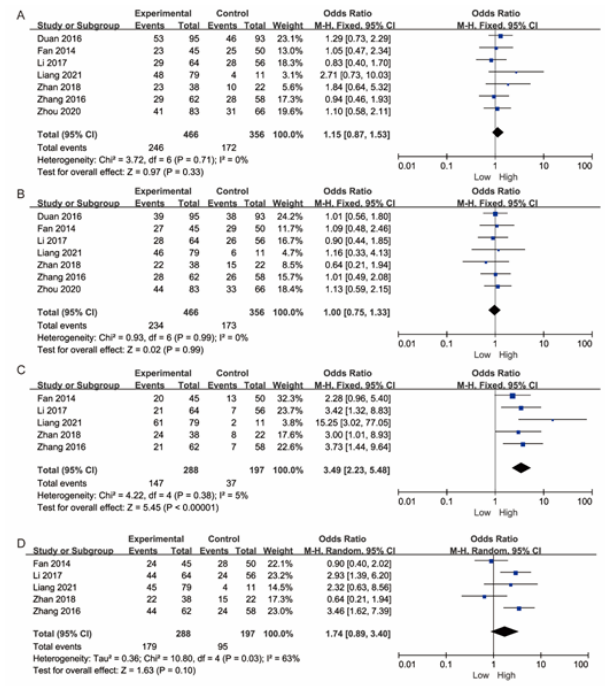

Figure 5. Meta-analysis of the clinicopathologic features in bladder cancer with the expression level of LncRNA MALAT1. (A) Age (≥ 60 vs. < 60); (B) Gender; (C) LNM (Yes vs. No); (D) TNM stage (III-IV vs. I-II); (E) Tumor size (≥ 3 cm vs.< 3 cm).

Discussion

Recent studies have revealed that lncRNAs are widely involved in a variety of biological processes in the human body and possess a variety of biological functions, including transcriptional interference, gene splicing, post-transcriptional regulation, cell cycle regulation, chromatin modification, epigenetic modifications and immune response (22). Studies have shown that LncRNA MALAT1 plays an important role in the occurrence and development of tumors (23). In our study, a meta-analysis was performed on the relationship between LncRNA MALAT1 and the prognosis of patients with bladder cancer.

This meta-analysis synthesized 7 included articles on the association between LncRNA MALAT1 and OS of bladder cancer patients. The results of our study show that bladder cancer patients with high lncRNA MALAT1 have a higher proportion of tumor node metastasis, distant metastasis, and lymph node metastasis than those with low lncRNA MALAT1 ($P < 0.05$). The OS of bladder cancer patients with high lncRNA MALAT1 was shorter than the patients with low lncRNA MALAT1 (HR = 2.34, 95% CI:1.61-3.38; P<0.001), which is consistent with previous studies (24). Compared with previous meta-analyses, this study retrieved more comprehensive literature with a larger sample size. Publication bias has a great influence on the reliability and authenticity of meta-analysis results, which often leads to overestimation of the comprehensive effect of the analysis. The linear regression model (Egger's test) is used to test the symmetry of the inverted funnel chart. If the P-value corresponding to the test statistic t is greater than 0.1, it can be inferred that the funnel chart is symmetrical, otherwise, it is asymmetrical. If the funnel chart is symmetrical, it means that there is no publication bias in the studies included in the meta-analysis, at least the potential bias has no substantial influence on the final result. Therefore, according to Egger's test of this Meta-analysis (Figure 4), it can be inferred that the result of this research is credible and reliable. Obviously, it is meaningful to determine the reasons for the inconsistency of research results. The quality heterogeneity between different studies may also be an important reason for the heterogeneity.

The downregulation of LncRNA MALAT1 resulted in decreased levels of epithelial-mesenchymal transition (EMT)-associated ZEB1, ZEB2, and Slug (25). Besides, lncRNA MALAT1 can promote EMT through the Wnt signaling pathway in vitro and enhance the invasion and metastasis of bladder cancer cells, therefore, inhibition of lncRNA MALAT1 can provide ideas for the treatment of bladder cancer. (26). Moreover, LncRNA MALAT1 is associated with bladder cancer cell invasion, migration, cell cycle, apoptosis and other properties. For example, M2 macrophages, as one of the major immune cells in the tumor microenvironment, increase the proliferation, migration, and invasion of bladder cancer cells. M2 macrophages trigger LncRNA MALAT1 overexpression

in an IL-8/STAT3-dependent manner, thereby promoting the development of bladder cancer (27). Down-regulation of LncRNA MALAT1 could inhibit the proliferation and invasion of bladder cancer cells by attenuating autophagy via the regulation of the AMPK/mTOR pathway (28). Therefore, exploring the effect of LncRNA MALAT1 on bladder cancer progression and related mechanisms is essential to better understand the pathogenesis of bladder cancer and to find new therapeutic targets.

However, the results of this study should be interpreted carefully. In the current research, there are still several limiting factors that must be considered. First, the cut-off value of LncRNA MALAT1 in this study is inconsistent among the studies, which may be the introduction of selection bias in the meta-analysis. Second, the bladder cancer patients involved in the study may receive different treatments, which may have an impact on survival rates. Third, patients included in the studies received follow-ups at different periods, which may have some influence on survival data. Finally, an international multicenter study with a larger sample size is needed to further confirm this in the future.

In conclusion, this study showed that in bladder cancer patients, the increase in lncRNA MALAT1 is related to a poor prognosis and higher lymph node metastasis. As a clinically accessible index, lncRNA MALAT1 should be identified as a biomarker with potential prognostic value in bladder cancer.

Conflict of Interests

The authors declared no conflict of interest.

Funding

This work was supported by the Ningbo Medical Science and Technology Planning Program (2020Y60).

References

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. Ca-Cancer J Clin 2021; 71(1): 7-33.
2. Lenis AT, Lec PM, Chamie K, Mshs MD. Bladder Cancer: A Review. Jama-J Am Med Assoc 2020; 324(19): 1980-1991.
3. Kirkali Z, Chan T, Manoharan M, et al. Bladder cancer: epidemiology, staging and grading, and diagnosis. Urology 2005; 66(6 Suppl 1): 4-34.
4. Martinez RR, Buisan RO, Ibarz L. Bladder cancer: Present and future. Med Clin-Barcelona 2017; 149(10): 449-455.
5. Bridges MC, Daulagala AC, Kourtidis A. LNCcation: lncRNA localization and function. J Cell Biol 2021; 220(2): e202009045.
6. Djebali S, Davis CA, Merkel A, et al. Landscape of transcription in human cells. Nature 2012; 489(7414): 101-108.
7. Schmitt AM, Chang HY. Long Noncoding RNAs in Cancer Pathways. Cancer Cell 2016; 29(4): 452-463.
8. Li ZX, Zhu QN, Zhang HB, Hu Y, Wang G, Zhu YS. MALAT1: a potential biomarker in cancer. Cancer Manag Res 2018; 10: 6757-6768.
9. Wu Y, Huang C, Meng X, Li J. Long Noncoding RNA MALAT1: Insights into its Biogenesis and Implications in Human Disease. Curr Pharm Design 2015; 21(34): 5017-5028.
10. Jiao D, Li Z, Zhu M, Wang Y, Wu G, Han X. LncRNA MALAT1 promotes tumor growth and metastasis by targeting miR-124/foxq1 in bladder transitional cell carcinoma (BTCC). Am J Cancer Res 2018; 8(4): 748-760.
11. Ren S, Liu Y, Xu W, et al. Long noncoding RNA MALAT-1 is a new potential therapeutic target for castration resistant prostate cancer. J Urology 2013; 190(6): 2278-2287.
12. Chang J, Xu W, Du X, Hou J. MALAT1 silencing suppresses prostate cancer progression by upregulating miR-1 and downregulating KRAS. Oncotargets Ther 2018; 11: 3461-3473.
13. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol 2010; 25(9): 603-605.
14. Tierney JF, Stewart LA, Ghersi D, Burdett S, Sydes MR. Practical methods for incorporating summary time-to-event data into meta-analysis. Trials 2007; 8: 16.
15. Duan W, Du L, Jiang X, et al. Identification of a serum circulating lncRNA panel for the diagnosis and recurrence prediction of bladder cancer. Oncotarget 2016; 7(48): 78850-78858.
16. Fan Y, Shen B, Tan M, et al. TGF-beta-induced upregulation of malat1 promotes bladder cancer metastasis by associating with suz12. Clin Cancer Res 2014; 20(6): 1531-1541.
17. Li C, Cui Y, Liu LF, et al. High Expression of Long Noncoding RNA MALAT1 Indicates a Poor Prognosis and Promotes Clinical Progression and Metastasis in Bladder Cancer. Clin Genitourin Canc 2017; 15(5): 570-576.
18. Liang T, Xu F, Wan P, et al. Malat-1 expression in bladder carcinoma tissues and its clinical significance. Am J Transl Res 2021; 13(4): 3555-3560.
19. Zhan Y, Du L, Wang L, et al. Expression signatures of exosomal long non-coding RNAs in urine serve as novel non-invasive biomarkers for diagnosis and recurrence prediction of bladder cancer. Mol Cancer 2018; 17(1): 142.
20. C. Zhang., Y. Cui., J. Chen., "Expression of metastasis-associated lung adenocarcinoma transcript 1 in bladder cancer and its clinical significance " China Journal of Modern Medicine, vol. 26, no. 17, pp. 116-120, 2016.
21. W. Zhou., G. Huang., Q. Yin., "Expression changes and significance of lncRNA MALAT1 and miR-146b-5p in bladder cancer tissue," Shandong medicine, vol. 60, no. 33, pp. 71-73, 2020.
22. Dykes IM, Emanueli C. Transcriptional and Post-transcriptional Gene Regulation by Long Non-coding RNA. Genom Proteom Bioinf 2017; 15(3): 177-186.
23. Goyal B, Yadav S, Awasthee N, Gupta S, Kunnumakkara AB, Gupta SC. Diagnostic, prognostic, and therapeutic significance of long non-coding RNA MALAT1 in cancer. Bba-Rev Cancer 2021; 1875(2): 188502.
24. Tian X, Xu G. Clinical value of lncRNA MALAT1 as a prognostic marker in human cancer: systematic review and meta-analysis. Bmj Open 2015; 5(9): e8653.
25. Chen L, Yao H, Wang K, Liu X. Long Non-Coding RNA MALAT1 Regulates ZEB1 Expression by Sponging miR-143-3p and Promotes Hepatocellular Carcinoma Progression. J Cell Biochem 2017; 118(12): 4836-4843.
26. Ying L, Chen Q, Wang Y, Zhou Z, Huang Y, Qiu F. Upregulated MALAT-1 contributes to bladder cancer cell migration by inducing epithelial-to-mesenchymal transition. Mol Biosyst 2012; 8(9): 2289-2294.
27. Zheng T, Ma G, Tang M, Li Z, Xu R. IL-8 Secreted from M2 Macrophages Promoted Prostate Tumorigenesis via STAT3/MALAT1 Pathway. Int J Mol Sci 2018; 20(1): 98.
28. Qi J, Chu Y, Zhang G, Li H, Yang D, Wang Q. Down-regulated LncR-MALAT1 suppressed cell proliferation and migration by inactivating autophagy in bladder cancer. Rsc Adv 2018; 8(54): 31019-31027.