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Decreased expression of lncRNA loc285194 as an independent prognostic marker in cancer: A systematic review and meta-analysis

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ABSTRACT

Background: Several studies have indicated that lncRNA loc285194 is aberrantly expressed in many types of cancer. This meta-analysis was performed to elucidate the potential role of lncRNA loc285194 as a prognostic marker in malignant tumors.

Methods: An electronic search of PubMed, Medline, Embase, and Web of Science was performed to identify all eligible papers related to the prognostic impact of lncRNA loc285194 expression in cancer. Hazard ratios (HR) and 95% confidence intervals (CI) were extracted from the included studies to explore the association between lncRNA loc285194 expression and patient overall and disease-free survival (OS & DFS). The odds ratios (ORs) were also calculated to assess the association between lncRNA loc285194 expression and clinicopathological parameters.

Results: A total of 14 eligible articles with 1215 patients were included in this meta-analysis. Meta-results revealed that low expression of lncRNA loc285194 was significantly correlated with poorer overall survival (OS; HR = 2.34; 95% CI, 1.78–3.06; P < 0.001) and disease-free survival (DFS; HR = 2.66; 95% CI, 1.95–3.64; P = 0.001) rates in cancer patients. Low lncRNA loc285194 expression was also found to be significantly associated with lymph node metastasis (LNM; OR = 2.17; 95% CI, 1.23–3.83; P = 0.007), and distant metastasis (DM; OR = 2.49; 95% CI, 1.26–4.91; P = 0.009).

Conclusions: This study demonstrated that decreased level of lncRNA loc285194 was associated with poor clinical outcomes for patients with different types of cancer, supporting a promising potential biomarker for prognosis and metastasis in human cancers.

1. Introduction

Cancer is the leading cause of morbidity and mortality worldwide. Several factors including the lack of effective therapies and late diagnosis are associated with the poor prognosis and reduced 5-year survival rate in patients with different types of cancers [1]. Despite continued efforts over the past few decades to develop specific and sensitive traditional protein-based biomarkers, little progresses have been made in early stage identification of cancers [2]. With the advances in functional genomics and advent of new nucleic acid-base molecules including cell free DNAs as well as exosome and non-coding RNAs over the last few years, particular interest has been found among researchers towards potentials cancer diagnostic and prognostic biomarkers [3]. Non-coding RNAs including; microRNAs (miRNAs), long non-coding RNAs (lncRNAs) and circular RNAs that are considered as “dark matters” without protein-coding function within the human genome, have recently attracted broad attention as biomarkers for cancer management [4–8].

LncRNAs are RNA molecules longer than 200bp with no or limited protein-coding potential [9,10]. To date, existing findings indicate that lncRNAs could play a critical role in regulation of various cellular biological processes such as proliferation, differentiation, apoptosis,

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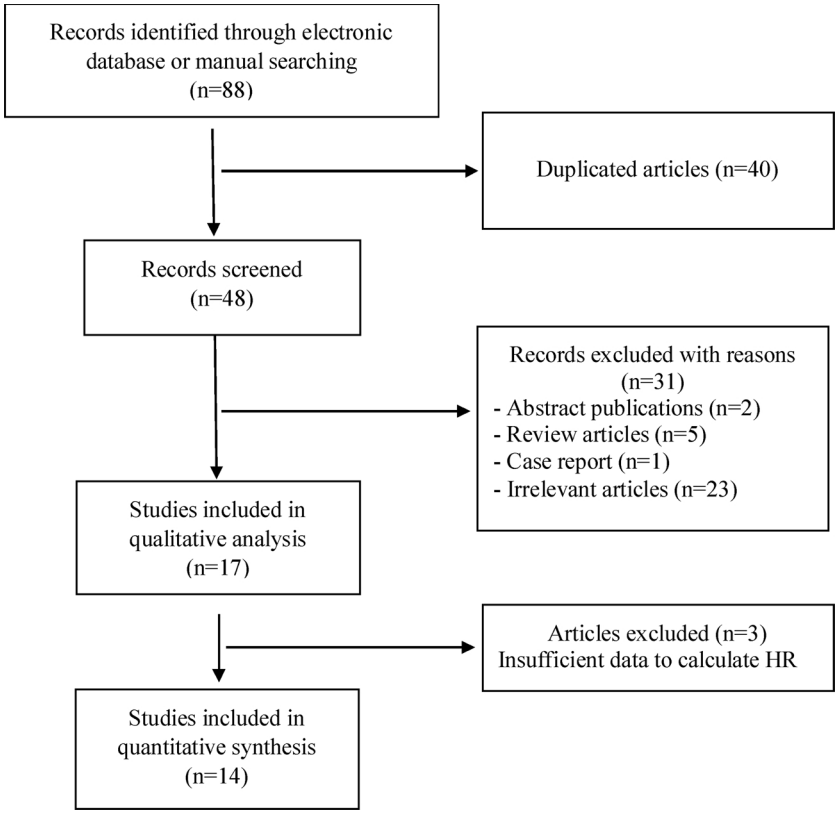

Fig. 1. Flow diagram of study selection process.

and cell cycle progression [11,12]. More importantly, many disease development processes including tumorigenesis, have also been attributed to deregulated lncRNA expression [13–15]. LncRNA have been reported to contribute in cancer development through modulation of oncogenic and tumor-suppressing pathways, representing fundamental regulators of cancer pathways, biomarkers of cancer outcomes and signatures for classification of different types of cancers [16,17]. Recently, some studies have been conducted to evaluate the value of lncRNAs in the diagnosis and treatment of various cancers. Indeed, a growing volume of literature has indicated that lncRNAs may serve as emerging molecular biomarkers in diagnosis or predictors of tumor response to treatment [18–20]. These novel biomarkers are essential for therapeutic decision-making and improving cancer patient outcomes.

LncRNA loc285194, also known as LSAMP antisense RNA 3 and tumor suppressor candidate 7 (TUSC7), is located on chromosome 3q13.31, and consists of four exons with 2105 nucleotide length. It was first reported as a tumor suppressor in osteosarcoma [21]. Overexpression of this lncRNA was shown to be capable of suppressing normal osteoblast cell proliferation and migration through regulating the expression of proteins controlling cell cycle and apoptosis as well as VEGF receptors. Recent studies have confirmed that down-regulation of lncRNA loc285194 is associated with tumor development and progression of several cancers such as esophageal squamous cell carcinoma, colorectal cancer, human pancreatic ductal adenocarcinoma, and hepatocellular carcinoma [22–25]. Most existing data suggest that lncRNA loc285194 might play important roles in pathogenesis of cancer and be a prognostic biomarker in some tumors. However, due to the limitation in discrete outcomes, sample size and research programs, a single study may not be able to reflect the facts accurately. Thus, conducting a systematic review and meta-analysis may clarify to what extent this molecule might be of prognostic significance. We, therefore conducted a meta-analysis of published studies to assess the potential prognostic value of lncRNA loc285194 expression in human cancers.

2. Material and methods

2.1. Literature search strategy and study selection

A systematic search of PubMed, Medline, Embase, and Web of Science was performed to identify all relevant published articles about lncRNA loc285194 as a prognostic factor for survival of patients with cancer. The search terms included “noncoding RNA”, “long non-coding RNA”, “lncRNA”, “lncRNA loc285194”, “LSAMP3”, “LSAMP-AS3”, “LSAMP antisense RNA3”, “tumor suppressor candidate 7”, “TUSC7”, “cancer”, “carcinoma”, “neoplasm”, “prognosis”, “prognostic”, “survival”, and “tumor” with limitations in “humans” and “English”, were used individually or/and in various combinations. The literature search ended on Mar 27, 2019. The titles and abstracts of all citations were screened independently by two authors (SR and HMM). Additionally, we manually searched the reference lists of all potentially eligible articles to find more relevant publications. We did not consider abstracts or unpublished reports and in the case of studies by the same author using the same case series, only the most recent or complete study was included. Animal studies and single case reports were also excluded. Studies meeting the following criteria were considered eligible: (1) studies on any type of human cancer; (2) the tissue expression of lncRNA loc285194 was determined; (3) any study investigating the relationship between lncRNA loc285194 expression and survival; (4) sufficient data was provided to estimate hazard ratios (HRs) for survival rates and their 95% confidence intervals (CI). On the other hand, studies that failed to meet the inclusion criteria and those with lack of sufficient data to calculate the HRs with 95% CI, duplicate publications, reviews, letters, case report, editorials, and comments were also excluded. If the data could not be extracted or calculated from the original article, the study was excluded.

Table 1
Basic characteristics of the included studies.

Study[ref]/year	Region	Tumor type	Sample size (n)	Age (Low/High)	Differentiation (Low/ High)	Tumor size (Low/High)	Male (Low/High) Female (Low/ High)	Clinical stage (Low/High)	loc285194 expression						Survival Analysis	HR (95% CI) Low vs. High	Method	NOS quality Score (%)
									High			Low						
									Total	LNM	DM	Total	LNM	DM				
Qi[23] 2013	China	CRC	81	< 56 35 ≥56 46	Well/ Moderate 35/23 Poorly/others 13/10	< 4 cm 16/20 ≥4 cm 32/13	21/18 27/15	I + II 22/23 III + IV 26/ 10	33	10	3	48	25	13	DSS Univ DSS Multi DFS	3.20 (1.32-7.77) 2.97 (0.71-12.5) 1.25 (1.05-4.30)	qRT-PCR	7
Tong[22] 2014	China	ESCC	142	≤55 8/10 > 55 63/ 61	G1 + G2: 42/57 G3/G4 29/14	≤5 cm 39/57 > 5 cm 32/14	49/45 22/26	I + II 26/40 III + IV 45/31	71	13	13	71	26	26	OS Multi DFS Multi	2.58 (1.40-4.76) 2.93 (1.66-5.18)	qRT-PCR	7
Ding[24] 2014	China	PDAC	85	< 60 16/21 ≥ 60 24/24	Well: 2/5 Moderate + poor 38/40	< 2 cm 6/5 ≥ 2 cm 34/40	23/33 17/12	I + II 6/26 III + IV 34/ 19	45	12	2	40	29	13	OS Uni OS Multi	2.77 (1.39-6.92) 2.42 (1.21-4.84)	qRT-PCR	7
Qi[30] 2015	China	GC	78	–	–	–	–	–	44	NS	NS	34	NS	NS	DFS Multi DSS Multi	2.86 (1.84-9.77) 1.81 (1.29-2.54)	qRT-PCR	5
Wang Z[25] 2016	China	NSCLC	112	≤60 43/37 > 60 13/19	Moderate-well 25/12 Poorly 31/44	≤3 cm 39/24 > 3 cm 17/32	25/32 31/24	I + II 41/22 III + IV 15/34	56	35	NS	56	30	NS	OS Multi DFS Multi	3.86 (2.26-6.59) 1.44 (1.22-3.40)	qRT-PCR	7
Wang Y[32] 2016	China	HCC	75	< 50 11/8 ≥ 50 27/29	NS	< 5 cm 21/22 ≥5 cm 19/13	24/27 14/10	I + II 28/15 III + IV 10/ 22	37	NS	–	38	NS	–	OS Multi DFS Multi	3.41 (1.39-8.37) 2.93 (1.23- 6.99)	qRT-PCR	8
Cong[33] 2016	China	OSA	82	–	–	–	–	–	13	–	–	69	–	–	OS Multi	3.19 (1.16-8.77)	qRT-PCR	6
Shang[34] 2016	China	Glioma	39	–	–	–	NS	–	20	–	–	19	–	–	OS Uni	2.81 (1.50-5.26)	qRT-PCR	7
Ma[35] 2017	China	Glioma	206	< 50 41/50 ≥ 50 63/52	NS	≤5 cm 67/71 > 5 cm 37/31	70/74 34/28	I + II 78/55 III + IV 26/ 47	102	–	–	104	–	–	DFS Multi OS Multi	1.53 (1.23-3.56) 1.32 (1.02-1.71)	qRT-PCR	7
Xu[36] 2017	China	CRC	63	–	–	–	–	–	10	–	–	53	–	–	OS Multi	2.92 (1.03-8.28)	qRT-PCR	7
Ren[37] 2017	China	CRC	40	–	–	–	–	–	13	–	–	27	–	–	OS Uni	1.27 (0.31-5.20)	qRT-PCR	7
Chang[38] 2018	China	ESCC	62	≤60 10/12 > 60 21/19	NS	≤5 cm 17/26 > 5 cm 14/5	23/20 8/11	I + II 10/19 III + IV 21/12	31	13	NS	31	19	NS	OS Uni	1.35 (0.50-3.65)	qRT-PCR	6
Zhou[39] 2019	China	NSCLC	56	< 60 14/17 ≥ 60 15/10	LUAD 16/15 LUSC 13/12	T1-T2 12/19 T3-T4 17/8	19/18 10/9	I + II 16/16 III + IV 13/11	27	9	3	29	11	2	OS Multi DFS Multi	5.02 (2.36-10.68) 6.66 (3.12-14.28)	qRT-PCR	7

(*continued on next page*)

Table 1 (*continued*)

Study[ref]/year	Region	Tumor type	Sample size (n)	Age (Low/High)	Differentiation (Low/High)	Tumor size (Low/High)	Male (Low/High) Female (Low/High)	Clinical stage (Low/High)	loc285194 expression						Survival Analysis	HR (95% CI) Low vs. High	Method	NOS quality Score (%)
									High			Low						
									Total	LNM	DM	Total	LNM	DM				
Yue[40] 2019	China	PC	94	< 60 20/21 ≥ 60 24/29	Moderate-well 32/28 Poorly 12/12	≤ 2 cm 26/28 > 2 cm 18/22	12/15 32/35	I + II 14/28 III + IV 30/22	50	24	20	44	32	31	OS Uni	1.20 (0.39-3.69)	qRT-PCR	6

NS: not stated; PDAC: pancreatic ductal adenocarcinoma; ESCC: esophageal squamous cell carcinoma; CRC: colorectal cancer; GC: gastric cancer; NSCLC: non-small-cell lung cancer; PC: pancreatic carcinoma; DSS: disease specific survival; OS: overall survival; DFS: disease free survival; Uni: Univariat analysis; Multi: Multivariate analysis; LNM: lymph node metastasis; DM: distant metastasis; LUAD: lung adenocarcinoma; LUSC: lung squamous cell carcinoma; Note: the dashes represent no data.

2.2. Data extraction and quality assessment

Two investigators (SR and HMM) independently assessed and scored the quality of the included studies according to the Newcastle-Ottawa Scale (NOS) and any disagreements were resolved through discussion with a third investigator (JA). Briefly, the following data were collected from each study: the first author's surname, year of publication, country of study, ethnicity, number of patients, tumor type, clinical stage of tumor, treatment data, study design, methods, cut-off values, disease-free survival (DFS) and overall survival (OS). If data from any of the earlier categories were not reported in the primary study, items were treated as "not stated". It was necessary that each eligible study must have been provided with enough information to extract the hazard ratio and related confidence intervals. If a study provided only Kaplan-Meier curve, the survival data was calculated based on the Kaplan-Meier survival curves using specific methods. All analyses were based on previously published studies; thus, no ethical approval or patient consent was required.

2.3. Statistical analysis

The strength of the association between lncRNA loc285194 expression and tumor parameters was measured by pooled hazard ratios or odds ratios (HRs or ORs) and their associated 95% confidence intervals (CI). HRs and 95% CIs were extracted from the published data or estimated using a survival information from Kaplan-Meier curves if not directly reported. The log HR and standard error (SE) were used to summarize overall survival outcome. Statistical heterogeneity among different studies was measured using the chi-square-based Cochran's Q and I^2 statistic with significant heterogeneity defined as an $I^2 > 50\%$, and $P < 0.05$. A random effect or fixed effect model was used depending on heterogeneity analysis results. If there was significant heterogeneity among the studies, the data were analyzed using a random effect model, otherwise, the fixed-effects model was applied. Galbraith plot analysis was also used to further explore which study or variables contribute substantial heterogeneity [26]. Moreover, sensitivity analyses were performed to test the effect of each individual study on the overall pooled results. Potential publication bias was evaluated using Begg's funnel plots and Egger's linear regression test. The statistical analysis was conducted using the Comprehensive Meta-Analysis software, and all P-values less than 0.05 were regarded as statistically significant.

3. Results

3.1. Literature search analysis

Process flow diagram of study screening for lncRNA loc285194 is shown in Fig. 1. A total of 88 articles were revealed in our initial search. After simultaneous review of titles and abstracts, 63 irrelevant or duplicate articles were excluded. Eight related studies were excluded because they were published as review, case report, or conference proceedings abstracts [27,28]. After careful inspection of the abstracts based on inclusion and exclusion criteria 17 papers were eligible for systematic review. Subsequently, data assessment of these articles, revealed 3 papers with insufficient data to estimate HR and/or OR for further analysis [21,25,29]. Finally, a total of 14 articles with 1215 patients were included in the current meta-analysis [22–24,30–40]. As shown in Table 1, all studies were conducted in China in a publication period between 2013 and 2019. A total of seven different types of cancer were included in this study (three colorectal cancers (CRC), two pancreatic carcinomas (PDAC/PC), two esophageal squamous cell carcinomas (ESCC), one osteosarcoma (OSC), one hepatocellular carcinoma (HCC), one gastric cancer (GC), two non-small-cell lung cancer (NSCLC), and two Gliomas). The NOS quality assessment confirmed that all included studies were of good quality (Table 1). LncRNA

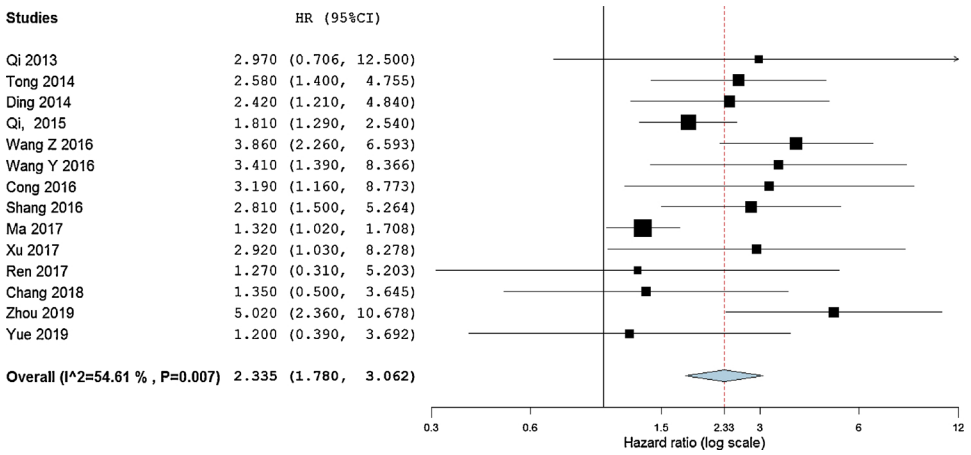

Fig. 2. Forest plot showing the association between loc285194 expression and OS in different cancer types.

Table 2
Results of association between low levels of lncRNA loc285194 and characteristics of patients with cancers.

Stratified analysis		No. of studies	No. of patients	Test of association		Test of heterogeneity		
				Pooled OR/HR (95% CI)	*P*-value	I^2 (%)	*P*-value	Model
Survival	OS	14	1215	2.34 (1.78-3.06)	< 0.001	54.61	0.007	R
	DFS	7	750	2.66 (1.95-3.64)	0.001	44.95	0.092	F
Cancer Type	Digestive system	8	645	1.97 (1.55-2.50)	0.001	0	0.795	F
	Others	6	570	2.90 (1.68-5.00)	0.001	79.82	0.001	R
	CRC	3	184	2.36 (1.14-4.86)	0.02	0	0.606	F
	NSCLC	2	168	4.09 (2.70-6.21)	0.001	0	0.772	F
	ESCC	2	204	2.11 (1.17-3.80)	0.013	15.58	0.276	F
	PC	2	179	1.97 (1.05-3.68)	0.034	7.74	0.298	F
	Glioma	2	269	1.82 (0.88-3.76)	0.109	79.01	0.029	R
Sample size	< 100	11	755	2.33 (1.83-2.96)	0.001	8.77	0.361	F
	> 100	3	460	2.29 (1.12-4.67)	0.023	86.21	0.001	R
Gender (male vs. female)		9	913	0.79 (0.60-1.04)	0.089	0.00	0.591	F
Age (High vs. Low)		8	832	1.10 (0.81-1.48)	0.553	8.27	0.366	F
Tumor size (large vs. small)		9	913	1.53 (0.87-2.70)	0.140	73.05	0.001	R
Histological grade (Poorly and others vs. well and moderately)		6	570	1.10 (0.55-2.19)	0.790	66.38	0.011	R
LNM (yes vs. no)		7	632	2.17 (1.23–3.83)	0.007	63.88	0.011	R
DM (yes vs. no)		5	458	2.49 (1.26-4.91)	0.009	41.317	0.146	F
Tumor stage (III + IV vs. I + II)		9	1013	1.26 (0.55–2.86)	0.590	88.15	< 0.001	R

OS: overall survival; DFS: disease free survival; F: Fixed effects model; R: random effects model; LNM: lymph node metastasis; DM: distant metastasis.

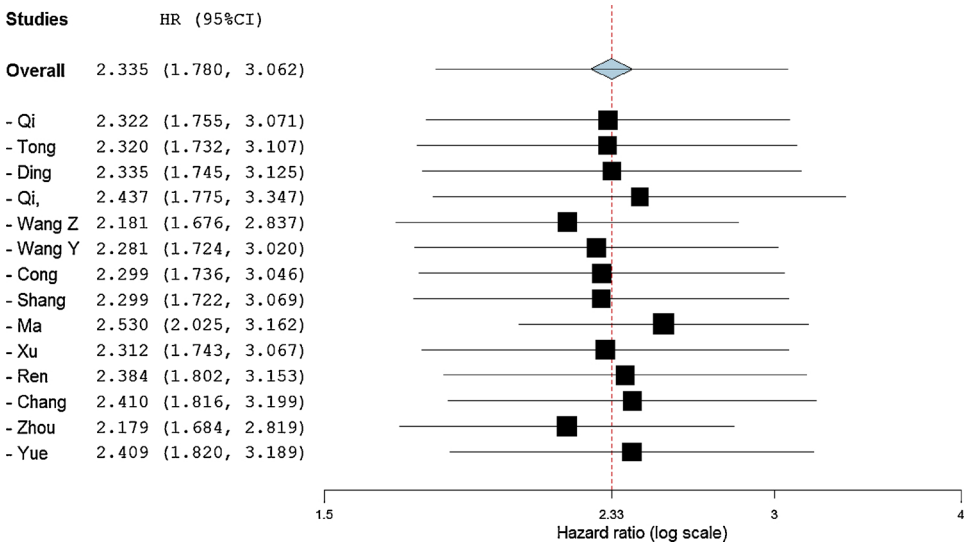

Fig. 3. Forest plot of the sensitivity analysis for the meta-analysis of OS in cancer patients.

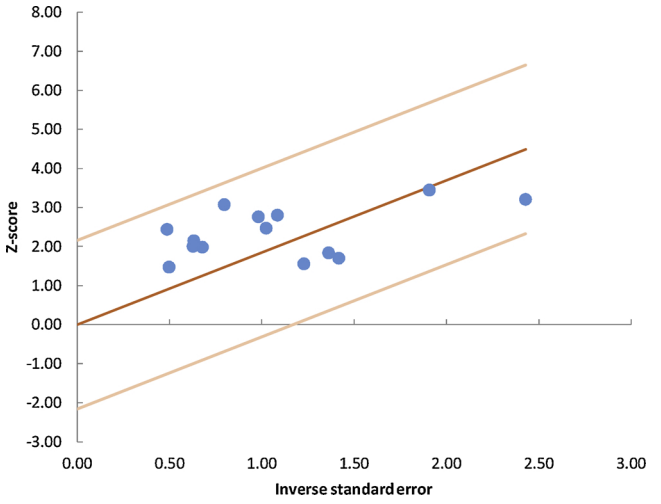

Fig. 4. Galbraith plots of the association between loc285194 expression and OS in different cancer types.

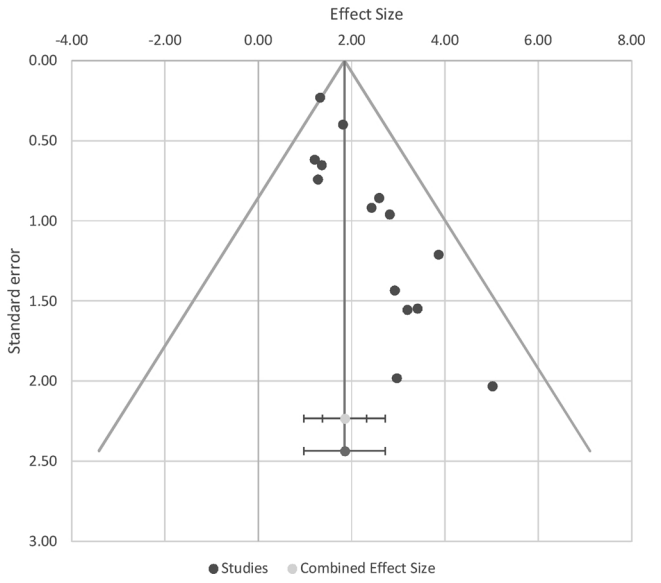

Fig. 5. Funnel plot analysis of potential publication bias for OS meta-analysis of loc285194.

loc285194 expression was measured in tumor specimens using the qRT-PCR method. According to arbitrary cut-off definitions, all included studies were grouped into two low and/or high lncRNA loc285194 expression groups. Data about lymph node metastasis (LNM), distant metastasis (DM), tumor stage, tumor size and histological grade were available in seven, five, nine, nine and six studies respectively.

3.2. Association between lncRNA loc285194 expression and OS

There were 14 studies reporting the overall survival (OS) of seven types of cancer based on lncRNA loc285194 expression levels in a total of 1215 patients. All studies conducted univariate or multivariate analysis of OS and a significant heterogeneity was observed (I^2 = 54.61%; P = 0.007). A cumulative meta-analysis using the random effect model assessing the pooled HR for the low lncRNA loc285194 expression group versus the high expression group, revealed that low expression of lncRNA loc285194 was in association to poorer survival rates, and lncRNA loc285194 expression had a protective role in cancer prognosis (HR = 2.34; 95% CI, 1.78–3.06; P < 0.001) (Fig. 2). Subgroup analyses were also conducted based on various cancer types, and sample sizes (Table 2). In stratified analyses by cancer types, decreased expression of lncRNA loc285194 was associated with poor OS in either patients with different kinds of digestive system carcinomas (individually or/and in overall) (HR = 1.97; 9 5% CI, 1.55–2.50; $p <$ 0.001) or other cancers (HR = 2.90; 95% CI, 1.68–5.00; P < 0.001). Subgroup analysis stratified by sample size using 100 patients as a threshold, was also revealed that low lncRNA loc285194 expression was significantly associated with poor OS both in studies with larger sample size (HR = 2.29; 95% CI, 1.12–4.67; P = 0.023) and smaller sample size (HR = 2.33; 95% CI, 1.83–2.96; P < 0.001) (Table 2). A significant association was also observed regard to the disease-free survival (DFS) reported in seven studies with a total of 750 patients (HR = 2.66; 95% CI, 1.95–3.64; $p =$ 0.001) (Table 2). These results indicated that elevated expression of lncRNA loc285194 could positively affect patients' survival.

3.3. Association between lncRNA loc285194 and clinicopathological characteristics

In order to explore the relationship between lncRNA loc285194 and clinicopathological features of cancer patients, further meta-analysis was performed using related data from studies which described clinicopathological features including LMN, DM, tumor stage, tumor size, depth of invasion, histological grade, age and sex distribution. Due to the lack of obvious heterogeneity among studies in, DM, depth of invasion, age and gender the fixed effects model was used to calculate the pooled OR with corresponding 95% CI. However, due to significant heterogeneity in studies regarding LNM (P = 0.011; I^2 = 63.88%), tumor stage (P = 0.001; I^2 = 88.15%), histological grade (P = 0.011; I^2 = 66.38%), and tumor size (P = 0.001; I^2 = 73.05%) (Table 2), the random-effects model was applied. From the combined results showed in Table 2, low expression of loc285194 was found to be significantly associated with LNM (OR = 2.17; 95% CI, 1.23–3.83; P = 0.007), and DM (OR = 2.49; 95% CI, 1.26–4.91; P = 0.001). However, no significant association was observed between the decreased lncRNA loc285194 expression and other clinicopathologic parameters including histological grade (OR = 1.10; 95% CI, 0.55–2.19; P = 0.790), tumor size (OR = 1.53; 95% CI, 0.87–2.70; $p =$ 0.790), gender (OR = 0.79; 95% CI, 0.60–1.04; P = 0.089), and age (OR = 1.10; 95% CI, 0.55–2.19; P = 0.553), (Table 2).

3.4. Sensitivity analysis and publication bias

To evaluate the stability of pooled results, a "Leave one out" sensitivity analysis was performed, and no single study altered the overall pooled HR or OR, indicating that summarized results were statistically robust (Fig. 3). Additionally, Galbraith plot analysis was also performed to detect the outliers as the potential sources of heterogeneity. However, the results indicated no individual study as the outlier and possible contributor to heterogeneity (Fig. 4).

Begg's funnel plot and Egger's regression asymmetry test were also used to examine whether there was a publication bias in analyzing the relationship between lncRNA loc285194 and overall survival. Both visual inspection of funnel plot (Fig. 5) and Egger test results revealed some evidence of significant small-study effects (t = 5.32; P = 0.014), suggestive of potential risk for publication bias.

4. Discussion

A growing body of evidence has demonstrated that lncRNAs are involved in various biological processes, including cell differentiation, development, and proliferation [41]. Multiple studies have also revealed the expression pattern of lncRNAs as a new player in various diseases, including cancer [42–44]. Aberrant expression of lncRNAs were affected the tumorigenesis and cancer progression and other clinical outcomes, through either oncogenic or tumor suppressive

pathways [45]. Considering the possible occurrence of metastases, including lymph node metastasis (LNM) and distant metastasis (DM) in most cancers, accurate prediction of metastasis risk is vital for improving patient outcomes. Therefore, it is imperative to identify novel and effective biomarkers with better diagnostic and prognostic performance for cancer disease. increasing numbers of studies in recent years have reported specific association of lncRNAs with tumor development, indicating their promising potential as biomarkers in cancer diagnosis, prognosis and monitoring [46]. The present meta-analysis was conducted to clarify the prognostic value of lncRNA loc285194 expression in all cancer types and also to examine its correlation with the main clinicopathological characteristics including LNM, DM, and clinical stage as important indicators of predicting prognosis.

Our data showed that low expression of lncRNA loc285194 was an indicator for advanced disease and poor prognosis in cancer patients. Moreover, combining HRs from Cox multivariate analyses demonstrated shorter OS and DFS in low lncRNA loc285194 expression group compared to those with high level, indicating that low expression of lncRNA loc285194 is likely to serve as an unfavorable prognostic factor for cancer patients. The pooled data illustrated that lncRNA loc285194 expression was also remarkably correlated with LNM (OR = 2.17; 95% CI, 1.23–3.83; P = 0.007), and DM (OR = 2.49; 95% CI, 1.26–46.91; P = 0.009) in these patients. In general, low expression of lncRNA loc285194 represents a significant risk factor for survival outcomes in the development of tumors in patients with different types of cancer and could develop as an independent factor for predicting the prognosis of cancer patients.

Almost all studies included in this meta-analysis have reported the significant correlation of lncRNA loc285194 expression with aggressive clinicopathological features and malignant potential in related cancers. Consistence with these results, previous researches have demonstrated an inhibitory role of lncRNA loc285194 overexpression for tumor cell growth both in vitro and in vivo [25,29]. In contrast, lncRNA loc285194 suppression by RNAi in tumor cell lines has promoted cell growth, providing more supporting evidence regarding its regulatory role as tumor suppressor. Continuous research has led to exploring the lncRNA loc285194 as a component of the p53-regulatory network [29]. Both experimental and clinical researches have confirmed down-regulation of this lncRNA in various tumor samples and different cell lines [22–25,29]. Existing data support the clinical significance of lncRNA loc285194 expression level as a novel prognostic biomarker in various cancers and a promising novel target for cancer therapy.

The present meta-analysis has some limitations which have to be pointed out when interpreting the conclusions. First, all included studies being from china, limited the generalizability to some extent. Second, the included papers, cancer types and patient numbers were small. Third, all included studies reported positive results, raised a probability of the bias toward more publication of positive results than those with negative results. Additional studies are needed to confirm the lncRNA loc285194 function in various cancers. Forth, the cut-off value for low or high levels of loc285194 varied in different studies, making difficult to reach a consensus value. Fifth, a difference in protocols for treatment after surgery in the various studies, might have a great impact on survival outcomes and thus result in some heterogeneity.

5. Conclusion

In conclusion, this study found that low lncRNA loc285194 expression was associated with LNM, DM, and poor OS/DFS in different types of cancer, supporting a promising potential biomarker for cancer prognosis. However, further comprehensive and large studies in different populations with various ethnicities are required to achieve a more persuasive conclusion.

Conflict of interest

The authors declare no conflicts of interest regarding the publication of this paper.

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