

Meta-analysis of the prognostic value of *lncRNA DANCR* for cancer patients in China

Yanghua Fan^{1,*}

Yu He^{2,*}

Xi Zhou^{2,*}

Yong Liu²

Fu Wang³

¹Department of Central Laboratory, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing, China; ²Department of Orthopedics, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing, China; ³Department of Orthopedic Surgery, Shandong Provincial Hospital Affiliated to Shandong University, Ji'nan, Shandong, China

*These authors contributed equally to this work

Background: Abnormal expression of long non-coding RNA anti-differentiation noncoding RNA (*lncRNA DANCR*) can frequently be detected in cancer. Because of this, it is of vital necessity to perform a meta-analysis to clarify the value of *lncRNA DANCR* as a prognostic marker in malignant tumors.

Methods: Related studies were retrieved from electronic databases including Web of Science, PubMed, and OVID, from inception to November 21, 2018. The HRs and corresponding 95% CIs were also calculated to explore the relationship of *lncRNA DANCR* expression with patient survival. Moreover, ORs were computed to assess the association of *lncRNA DANCR* expression with the pathological parameters.

Results: A total of 14 studies involving 1,117 patients were included in this meta-analysis. The pooled HR suggested that high *lncRNA DANCR* expression was correlated with poor overall survival (OS; HR =1.85, 95% CI: 1.56–2.18) and disease-free survival (DFS; HR =2.49, 95% CI: 1.75–3.56) in cancer patients. Besides, High *lncRNA DANCR* expression was related to poor histological grade (PHG; OR =2.01, 95% CI: 1.08–3.75), high tumor stage (HTS; OR =3.52, 95% CI: 1.67–7.43), lymph node metastasis (LNM; OR =3.47, 95% CI: 1.42–8.49), and distant metastasis (DM; OR =4.76, 95% CI: 2.39–9.51). However, no evidence of obvious asymmetry was found for DFS (Pr>|z|=0.308), PHG (Pr>|z|=0.707), LNM (Pr>|z|=0.174), and DM (Pr>|z|=0.734) using Begg's funnel plot.

Conclusion: Our findings suggest that high *lncRNA DANCR* expression can predict poor OS, DFS, PHG, HTS, LNM, and DM in cancer patients, implying that high *lncRNA DANCR* expression may potentially serve as a new indicator for poor prognosis and metastasis in cancer.

Keywords: lncRNA, DANCR, neoplasms, prognosis, metastasis

Introduction

Recent report demonstrates that, the US has witnessed about 1.7 million new cancer cases and 600,000 cancer-related deaths in 2017.¹ Nevertheless, the 5-year survival of most cancers remains dismally low, and a large number of scientists are devoting themselves to looking for new biomarkers to determine or diagnose cancer prognosis.

lncRNA, which lacks a meaningful open reading frame, is defined as the transcribed RNA molecule that is >200 nucleotides in length, which has possessed many important functions in disease, such as posttranscriptional, transcriptional, and epigenetic regulation.^{2,3} In addition, abnormal lncRNA expression is currently recognized to be related to various cancer types.⁴⁻⁷ For instance, some lncRNAs play crucial parts in metastasis, invasion, and proliferation of cancer cells, indicating that lncRNA may serve be a useful marker for predicting cancer prognosis.⁸⁻¹⁰

Correspondence: Yong Liu
Department of Orthopaedics, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Sciences, No. 1 Shuaifuyuan, Dongcheng District, Beijing 100730, China
Email pumchliuyong@163.com

Fu Wang
Department of Orthopedic Surgery, Shandong Provincial Hospital Affiliated to Shandong University, No. 324 Jingwu Road, Ji'nan Shandong, 250021, China
Email sphwangfu163@126.com

Typically, the *lncRNA DANCR* was discovered by Kretz et al in 2012, which was originally deemed to be essential for the dedifferentiation of epidermal cells.¹¹ Besides, recent studies reveal that DANCR plays a crucial role in the differentiation of periodontal ligament stem cells into osteoblasts, which can also promote tumor cell dissemination and metastasis formation.^{12–14} Moreover, *lncRNA DANCR* is also suggested in some studies to be correlated with different tumor biological parameters, such as tumor growth, metastasis, and progression.^{15–17} Metastasis and prognosis may be affected by *lncRNA DANCR*; nonetheless, a majority of existing studies are limited by their small sample sizes and discrete outcomes. As a consequence, an updated meta-analysis was performed in this study to determine the prognostic value of *lncRNA DANCR* in cancer patients.

Materials and methods

Literature collection

In accordance with the standard guidelines for meta-analyses,^{18,19} related articles that served *lncRNA DANCR* as a prognostic biomarker for the survival of cancer patients were systemically retrieved from some online databases by two authors independently from inception to November 21, 2018. Meanwhile, text words and Mesh strategies were adjusted based on the databases in this retrieval, including the following terms (“Long non-coding RNA differentiation antagonizing non-protein coding RNA” or “*lncRNA DANCR*” or “*lncRNA ANCR*”) and (“recurrence” or “outcome” or “survival”, “cancer” or “neoplasm” or “tumor” or “carcinoma”, “prognosis” or “prognostic”). Moreover, the reference lists of relevant articles were also manually retrieved during retrieval, so as to avoid missing any potentially eligible studies.

Study selection

All the included studies were then evaluated, and data were extracted by two scholars independently. Typically, the study inclusion criteria were as follows: 1) studies in which all tumors were confirmed by histological or pathological examinations; 2) studies in which the *lncRNA DANCR* expression levels in human tumor tissues were measured; 3) studies in which patients were grouped in accordance with different *lncRNA DANCR* expression levels, and the cutoff values of high and low DANCR expression might be the median or mean of all samples in their study; and 4) studies with sufficient original data for statistical analyses of pathological or patient survival parameters with *lncRNA DANCR* expression.

In addition, the study exclusion criteria were shown below: non-human studies and non-English studies; edito-

rials, reviews, expert opinions as well as letters; database analysis without original data; and studies mentioning functions and molecular structure of *lncRNA DANCR* only.

Date extraction

Data from the original articles were independently examined and extracted by two reviewers, and any disagreement between them during the process of literature assessment was settled by the consensus with a third reviewer. A series of data were collected in this meta-analysis, including surname of the first author, publication year, country, tumor type, sample size, number of patients with LTS, PHG, HTS, LNM and DM, reference gene and detection method of *lncRNA DANCR*, as well as HRs and 95% CIs of elevated *lncRNA DANCR* expression for OS and DFS.

Statistical methods

The Stata version 12.0 software was adopted for all statistical analyses. In addition, the heterogeneity was also measured in this meta-analysis using Q and I^2 tests. The test results had indicated the presence of significant heterogeneity in this research ($I^2 \geq 50\%$, and $P < 0.1$);²⁰ therefore, the random effect model should be adopted. Besides, the potential publication bias was also assessed by Egger’s test and Begg’s funnel plot. The pooled ORs and HRs should be extracted from the published data; typically, the crude data should be adopted if the HRs could not be obtained directly from the publications. Besides, the survival information extracted from Kaplan–Meier curves should be adopted to estimate the HRs when they were not directly reported in the studies. To make a summary about the outcomes of survival, both SE and the log HR should be collected.²¹ Moreover, 95% CIs and ORs should be combined to assess the relationship of clinicopathological parameters with *lncRNA DANCR*.

Results

Study characteristics

Details about the screening process are shown in Figure 1. In accordance with the exclusion and inclusion criteria, 14 studies involving 1,117 patients were enrolled into this meta-analysis.^{22–35} Characteristics of the 14 studies included in this meta-analysis are summarized in Table 1. As could be observed, the sample size in the 14 studies ranged from 34 to 135, with an average of 79.57. Besides, all the enrolled studies were published between 2015 and 2018 and were carried out in China. Among these studies, respectively, one study had focused on CVR,²⁵ TNBC,²⁹ RB,³⁰ HCC,³⁴ and BC;³⁵ three concentrated on GC;^{22,27,28} two focused

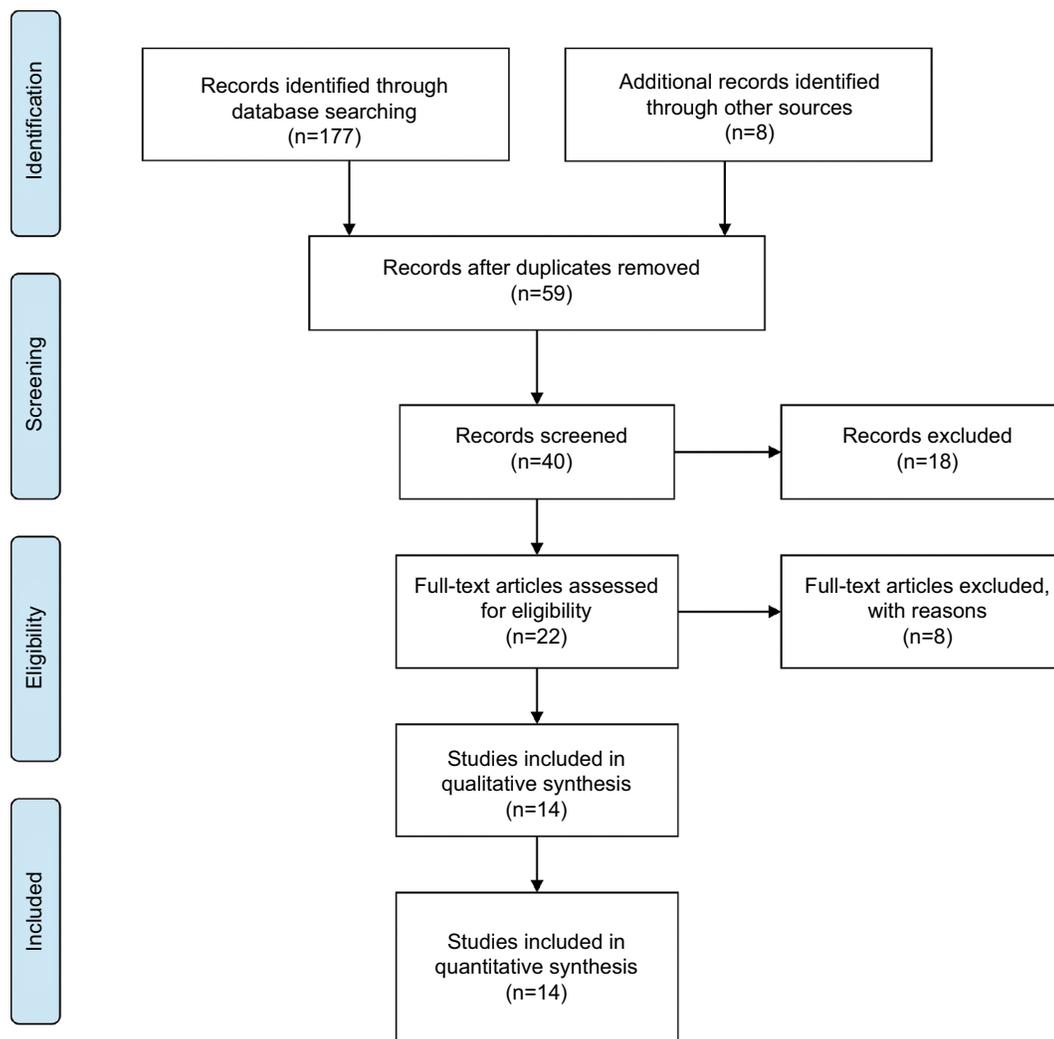


Figure 1 Flowchart presented the steps of study selection in this meta-analysis.

on OSC;^{23,32} two on glioma;^{24,33} and two on CRC.^{26,31} All clinical pathological parameters were dependent on the pathology. Moreover, it was found that the reference genes of *lncRNA DANCR* were different among these studies, which had included *GAPDH*,^{23–27,29–34} *β-actin*,^{22,35} and small nuclear RNA *U6*.²⁸ Moreover, the thresholds of high and low *lncRNA DANCR* expression levels, including the median and average *lncRNA DANCR* expression, were also different among these studies.

Association between the *lncRNA DANCR* expression level and survival

To assess the role of *lncRNA DANCR* in OS for cancer patients, cumulative meta-analysis was carried out in this research. As shown, the relationship of OS with *lncRNA DANCR* was reported in ten studies enrolling 839 patients

(Table 2). Meanwhile, the fixed effects model was adopted since there was no significant heterogeneity ($I^2=0.0\%$, $P_Q=0.728$). The results suggested that the OS in cancer patients was markedly related to the *lncRNA DANCR* expression (pooled HR =1.85, 95% CI: 1.56–2.18; Figure 2A). Besides, sensitivity analysis was also carried out, which had confirmed the robustness of these results (Figure 2B). Subsequently, subgroup analyses stratified by cancer type, sample size, NOS score, and HR statistic method were also carried out (Table 3, Figure 3).

Moreover, cumulative meta-analysis was also performed to determine the role of *lncRNA DANCR* in DFS among the 330 cancer patients recruited into the eligible studies (Figure 4). The results revealed that *lncRNA DANCR* was correlated with DFS (pooled HR =2.49, 95% CI: 1.75–3.56) in cancer patients upon statistical analyses. Similarly, the

Table 1 The basic information and data of all included studies in the meta-analysis

Reference	Year	Country	Tumor type	Sample size (n)	High <i>lncRNA DANCR</i> expression (n)					Low <i>lncRNA DANCR</i> expression (n)					Reference gene	Cutoff	Detection method	
					Total	LTS	PHG	HTS	LNM	DM	Total	LTS	PHG	HTS				LNM
Hao et al ²²	2017	China	GC	118	46	6	24	18	20	-	72	37	36	52	48	-	β -actin	PCR
Jiang et al ²³	2017	China	OSC	34	19	12	-	-	-	12	15	6	-	-	5	-	GAPDH	PCR
Li and Zhou ²⁴	2018	China	Glioma	86	43	-	-	38	-	-	43	-	-	21	-	Mean	GAPDH	PCR
Liang et al ²⁵	2019	China	CVR	65	33	23	-	21	18	-	32	11	-	7	4	Median	GAPDH	PCR
Liu et al ²⁶	2015	China	CRC	104	52	24	29	40	21	21	52	21	14	27	8	Median	GAPDH	PCR
Mao et al ²⁷	2017	China	GC	60	30	13	-	18	23	-	30	16	-	9	13	Median	GAPDH	PCR
Pan et al ²⁸	2018	China	GC	65	40	27	25	33	36	1	25	6	17	13	0	-	U6	PCR
Sha et al ²⁹	2017	China	TNBC	63	32	10	19	20	17	-	31	10	6	6	5	Median	GAPDH	PCR
Wang et al ³⁰	2018	China	RB	57	29	-	-	-	-	-	28	-	-	-	-	Median	GAPDH	PCR
Wang et al ³¹	2018	China	CRC	47	26	20	8	21	22	23	21	11	6	11	9	Median	GAPDH	PCR
Wang et al ³²	2018	China	OSC	95	72	49	-	46	-	50	23	7	7	8	-	Mean	GAPDH	PCR
Yang et al ³³	2018	China	Glioma	82	41	-	-	-	-	-	41	-	-	-	-	Median	GAPDH	PCR
Yuan et al ³⁴	2016	China	HCC	135	68	-	-	-	-	-	67	-	-	-	-	Median	GAPDH	PCR
Zhan et al ³⁵	2018	China	BC	106	70	44	45	59	11	-	36	20	13	21	-	β -actin	PCR	

Note: The dashes represent no data.
Abbreviations: BC, bladder cancer; CRC, colorectal cancer; CVR, cervical cancer; DM, distant metastasis; GAPDH, glyceraldehyde-3-phosphate dehydrogenase; GC, gastric cancer; HCC, hepatocellular carcinoma; HTS, high tumor stage; *lncRNA DANCR*, long non-coding RNA anti-differentiation noncoding RNA; LNM, lymph node metastasis; LTS, larger tumor size; OSC, osteosarcoma; PHG, poor histological grade; RB, retinoblastoma; TNBC, triple negative breast cancer.

fixed effects model was employed due to the insignificant heterogeneity.

These results suggested that the shorter OS and DFS in cancer patients might be associated with higher *lncRNA DANCR* expression. As a result, it could be concluded that *lncRNA DANCR* was an independent factor of the survival for cancer patients.

Association between the *lncRNA DANCR* expression level and LTS

Figure 5A shows the association between LTS and *lncRNA DANCR* expression from ten studies involving 757 patients. Specifically, the random-effects model was adopted due to the presence of a significant heterogeneity among the eligible studies ($I^2=79.4\%$, $P_Q=0.000$). Our results had revealed a pooled OR of 1.63 (95% CI: 0.80–3.31; high vs low *lncRNA DANCR* expression). Moreover, sensitivity analysis of all included studies was also performed, and the OR of high to low expression groups was 2.10 (95% CI: 1.25–3.54) after the study by Hao et al²² was excluded ($I^2=56.6\%$, $P_Q=0.018$) (Figure 5B and C).

Conforming to the abovementioned results, no significant difference was detected in the LTS incidence between two groups, but additional studies were needed to confirm the association between *lncRNA DANCR* and LTS in cancer patients.

Association between the *lncRNA DANCR* expression level and PHG

In this research, data regarding the association between the *lncRNA DANCR* expression and PHG had been collected from six eligible studies involving 503 cancer patients, and the random-effects model was adopted as a result of the significant heterogeneity ($I^2=61.4\%$, $P_Q=0.024$). Besides, the OR of high to low *lncRNA DANCR* expression groups was 2.10 (95% CI: 1.08–3.75, Figure 6A). Typically, the heterogeneity had disappeared ($I^2=24.2\%$, $P_Q=0.266$) after two studies were removed in sensitivity analysis, with the OR of high to low expression groups of 3.14 (95% CI: 1.95–5.05) (Figure 6B and C).

In accordance with these results, a significant difference was noted in the incidence of PHG between two groups, indicating that the risk of PHG was remarkably correlated with high *lncRNA DANCR* expression.

Association between the *lncRNA DANCR* expression level and HTS

In this meta-analysis, the correlation between HTS and *lncRNA DANCR* expression was detected in ten eligible

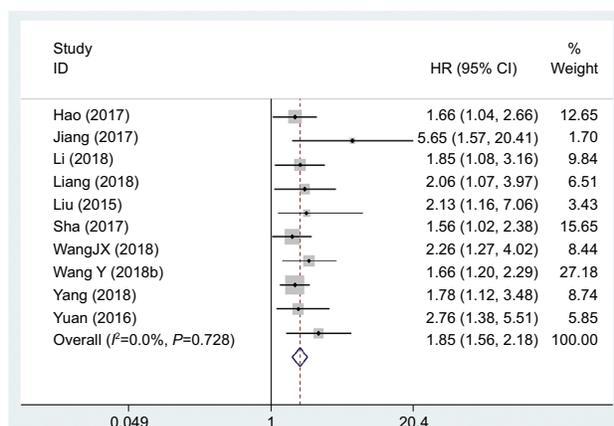
Table 2 Survival data of studies included in the meta-analysis

Reference	Year	Country	Tumor type	Sample size (n)	Method	OS, HR (95% CI)	DFS, HR (95% CI)	HR statistic	NOS
Hao et al ²²	2017	China	GC	118	Multivariate	1.66 (1.0363–2.6590)	NA	Survival curve	8
Jiang et al ²³	2017	China	OSC	34	Multivariate	5.65 (1.565–20.408)	3.759 (1.179–12.048)	Data in paper	7
Li and Zhou ²⁴	2018	China	Glioma	86	Multivariate	1.85 (1.0844–3.1562)	NA	Survival curve	7
Liang et al ²⁵	2019	China	CVR	65	Multivariate	2.06 (1.0683–3.9724)	NA	Survival curve	7
Liu et al ²⁶	2015	China	CRC	104	Multivariate	2.131 (1.157–7.058)	2.397 (1.385–7.279)	Data in paper	8
Mao et al ²⁷	2017	China	GC	60	NA	NA	NA	NA	8
Pan et al ²⁸	2018	China	GC	65	NA	NA	NA	NA	7
Sha et al ²⁹	2017	China	TNBC	63	Multivariate	1.56 (1.02–2.38)	NA	Survival curve	8
Wang et al ³⁰	2018	China	RB	57	Multivariate	2.26 (1.2694–4.0238)	2.84 (1.3068–6.1721)	Survival curve	6
Wang et al ³¹	2018	China	CRC	47	NA	NA	NA	NA	8
Wang et al ³²	2018	China	OSC	95	Multivariate	1.66 (1.2037–2.2893)	NA	Survival curve	7
Yang et al ³³	2018	China	Glioma	82	Multivariate	1.783 (1.121–3.4821)	NA	Data in paper	6
Yuan et al ³⁴	2016	China	HCC	135	Multivariate	2.757 (1.379–5.514)	2.228 (1.359–3.653)	Data in paper	6
Zhan et al ³⁵	2018	China	BC	106	NA	NA	NA	NA	7

Note: NA represents no data.

Abbreviations: BC, bladder cancer; CRC, colorectal cancer; CVR, cervical cancer; DFS, disease-free survival; GC, gastric cancer; HCC, hepatocellular carcinoma; NOS, Newcastle–Ottawa Scale; OS, overall survival; OSC, osteosarcoma; RB, retinoblastoma; TNBC triple negative breast cancer.

A



B

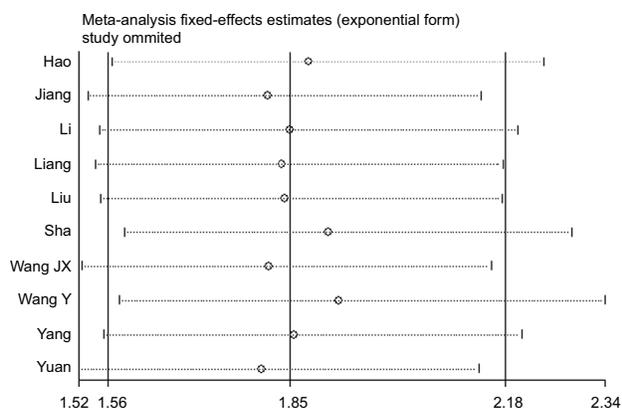


Figure 2 Forest plot (A) and sensitivity analysis (B) showed the relationship between *lncRNA DANCR* expression level and OS in cancer.

Abbreviations: *lncRNA DANCR*, long non-coding RNA anti-differentiation noncoding RNA; OS, overall survival.

studies recruiting 809 patients. Similarly, the random effects model would be adopted ($I^2=81.4\%$, $P_Q=0.000$). The results discovered that HTS in cancer patients was notably related to high *lncRNA DANCR* expression (pooled OR =3.52, 95% CI: 1.67–7.43, Figure 7A). In addition, the heterogeneity had disappeared in sensitivity analysis after the study by Hao et al²² was excluded ($I^2=0.0\%$, $P_Q=0.905$), and the OR of high to low *lncRNA DANCR* expression groups was 4.67 (95% CI: 3.30–6.60) (Figure 7B and C).

According to the analysis results, compared with the low *lncRNA DANCR* expression group, the tumor stage in high *lncRNA DANCR* expression group was markedly higher, demonstrating that the risk of HTS was evidently correlated with high *lncRNA DANCR* expression.

Association between the *lncRNA DANCR* expression level and LNM

In this research, data collected from eight eligible studies involving 628 cancer patients were also analyzed, and the random effects model had been adopted based on the significant heterogeneity ($I^2=80.4\%$, $P_Q=0.000$). Additionally, the OR of to low *lncRNA DANCR* expression groups was 3.47 (95% CI: 1.42–8.49, Figure 8A). Consistent with the results of previous sensitivity analysis, the heterogeneity had disappeared ($I^2=0.0\%$, $P_Q=0.693$) after the study by Hao et al²² was removed (Figure 8B and C).

In accordance with these results, a significant difference was noted between two groups in terms of LNM incidence.

Table 3 Subgroup analysis of OS by tumor type, sample size, NOS score, and HR statistic method

Subgroup analysis	No. of studies	No. of patients	Pooled HR (95% CI)	Heterogeneity	
				I ² (%)	P-value
Total	10	839	1.85 (1.56–2.18)	0.0	0.728
Cancer type					
Digestive system cancer	3	357	1.98 (1.38–2.83)	0.0	0.487
Non-digestive system cancer	7	482	1.81 (1.50–2.19)	0.0	0.610
Sample size					
Number >90	4	452	1.79 (1.41–2.28)	0.0	0.584
Number ≤90	6	387	1.90 (1.50–2.40)	0.0	0.540
NOS score					
NOS >7	3	285	1.65 (1.23–2.23)	0.0	0.829
NOS ≤7	7	554	1.94 (1.59–2.38)	0.0	0.548
HR statistic					
Survival curve	6	484	1.75 (1.45–2.11)	0.0	0.917
Data in paper	4	355	2.31 (1.59–3.37)	0.0	0.400

Abbreviations: NOS, Newcastle–Ottawa Scale; OS, overall survival.

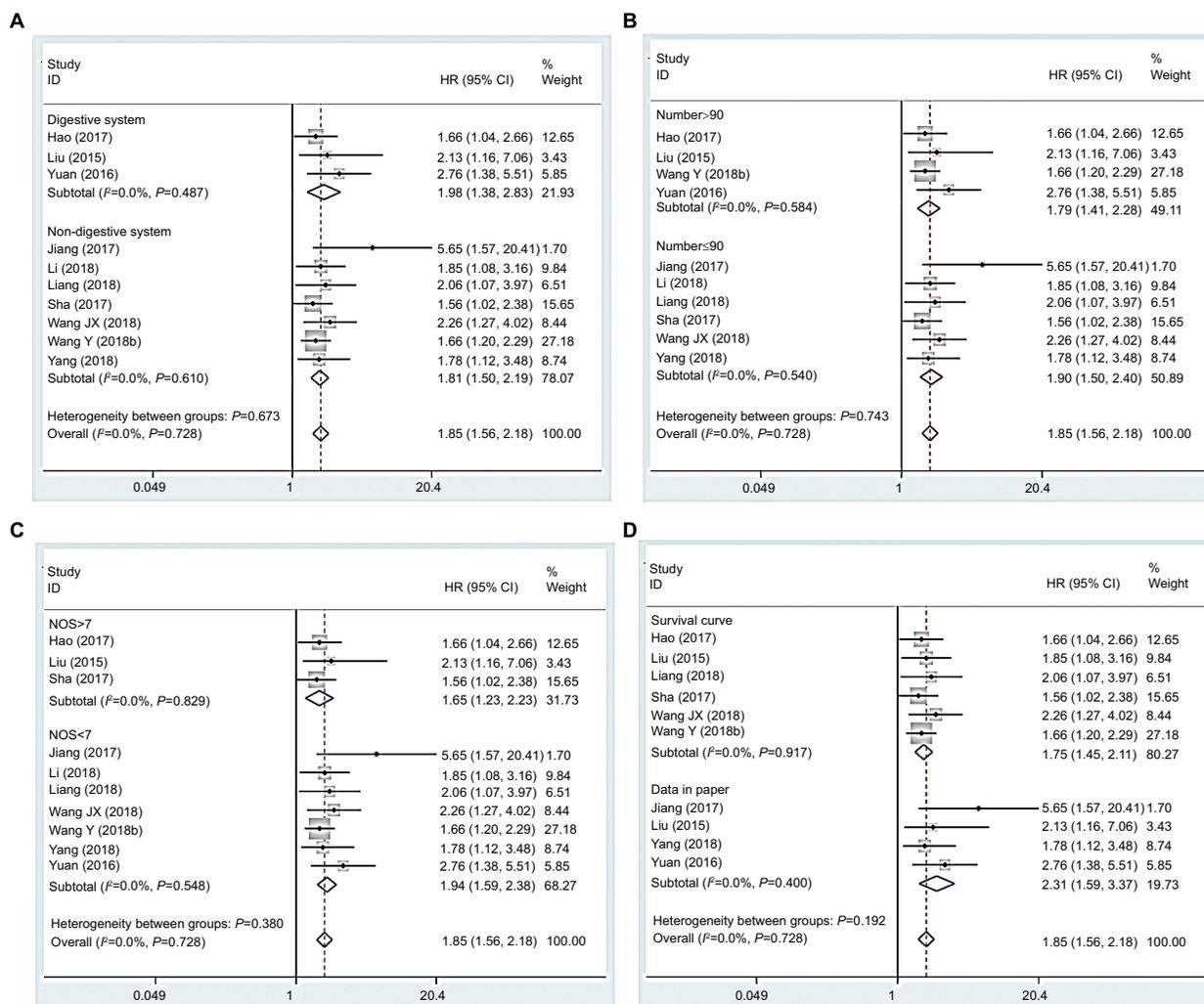


Figure 3 Forest plots of subgroup analysis for OS of patients with cancer.

Notes: Subgroup analysis by tumor type (A), sample size (B), NOS score (C), and HR statistic method (D).

Abbreviations: NOS, Newcastle–Ottawa Scale; OS, overall survival.

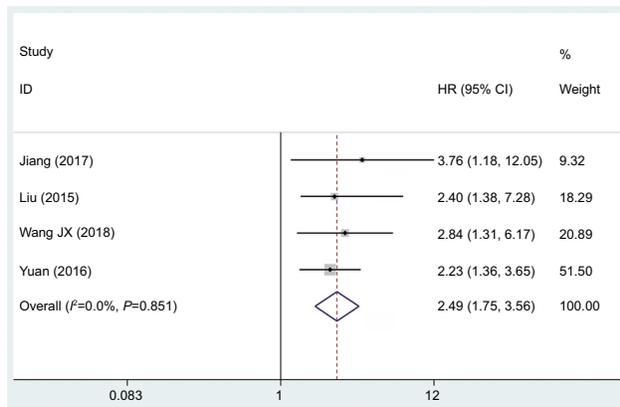


Figure 4 Forest plot showed the relationship between *lncRNA DANCR* expression level and DFS in cancer.

Abbreviations: DFS, disease-free survival; *lncRNA DANCR*, long non-coding RNA anti-differentiation noncoding RNA.

As far as cancer patients were concerned, high *lncRNA DANCR* expression was markedly correlated with greater susceptibility to LNM.

Association between the *lncRNA DANCR* expression level and DM

In this meta-analysis, the correlation of DM with the *lncRNA DANCR* expression level was examined in four eligible studies including 241 patients, and the fix effects model was adopted due to the limited heterogeneity (I²=0.0%, P_Q=0.666). The OR of high to low *lncRNA DANCR* expression groups was 4.76 (95% CI: 2.39–9.51, Figure 9). Consistent with these results, the DM incidence was significantly different between two groups, revealing that high *lncRNA DANCR* expression could remarkably predict a higher tendency to develop DM in cancer patients.

Publication bias

Subsequently, the Begg’s funnel plot was conducted in this study to evaluate the potential publication bias. Figure 10 shows no evidence of obvious asymmetry for DFS (Pr>|z|=0.308), LTS (Pr>|z|=0.283), PHG (Pr>|z|=0.707), LNM (Pr>|z|=0.174), and DM (Pr>|z|=0.734). However, significant publication bias was detected for OS (Pr>|z|=0.004) and HTS (Pr>|z|=0.007).

Discussion

Cancer still poses a serious threat to human health, which is gradually increased in recent years in terms of morbidity.¹ Nonetheless, the exact metastasis mechanism in cancer patients remains unclear despite that metastasis is an important indicator of poor prognosis.^{36,37} Therefore, it is necessary

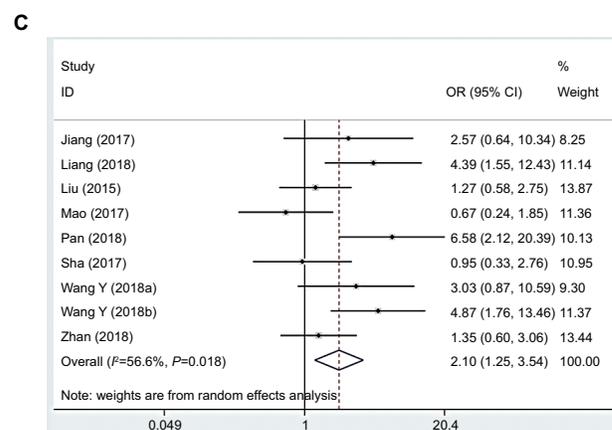
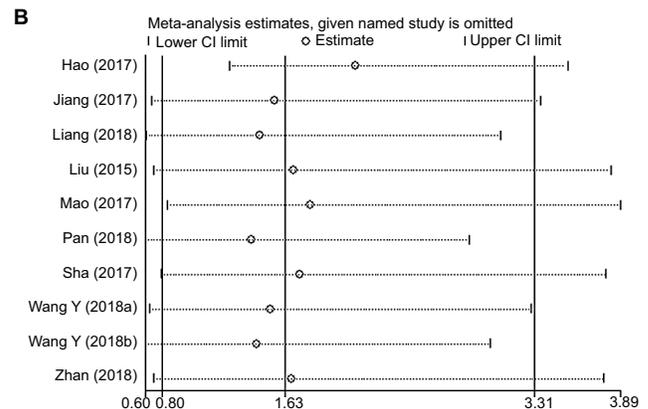
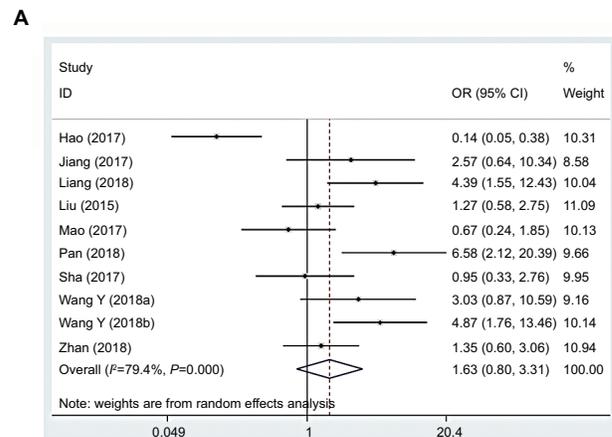


Figure 5 Forest plot (A), sensitivity analysis (B), and the forest plot of sensitivity analysis (C) showed the association between LTS and *lncRNA DANCR* expression level in cancer.

Abbreviations: *lncRNA DANCR*, long non-coding RNA anti-differentiation noncoding RNA; LTS, larger tumor size.

to identify new molecular markers to predict tumor metastasis at present, since they may play critical roles in treating and predicting cancer.³⁸ lncRNAs, one of these molecular markers, can affect tumor initiation, progression, and occurrence, which can easily collect the useful biomarkers for cancer monitoring and diagnosis.^{39–41}

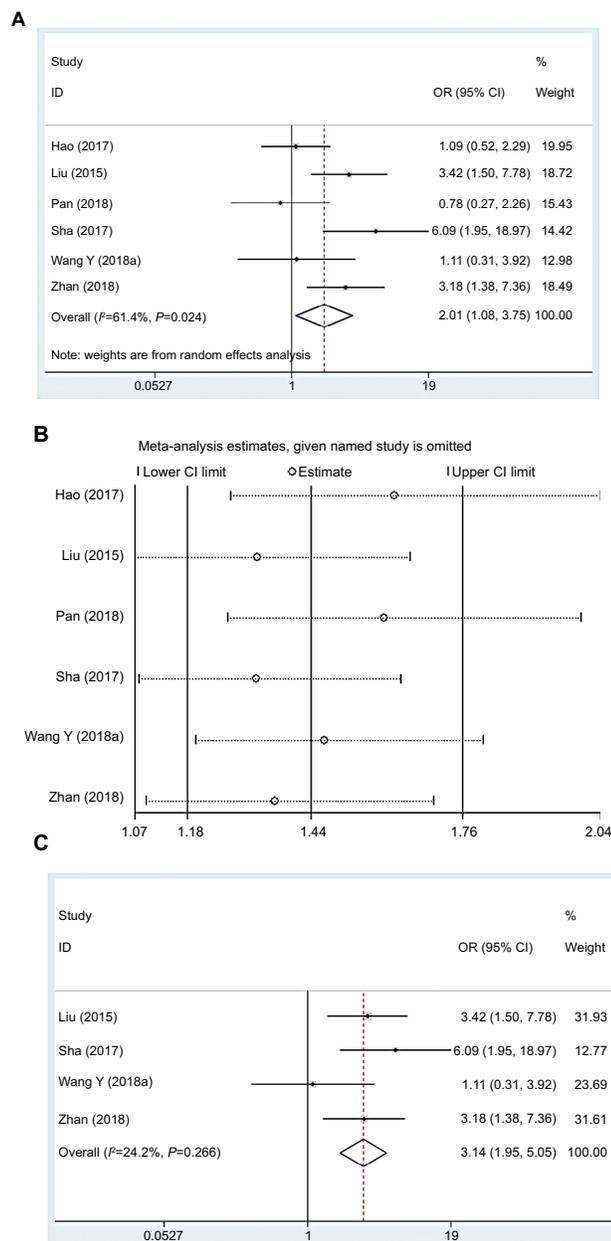


Figure 6 Forest plot (A), sensitivity analysis (B), and the forest plot of sensitivity analysis (C) showed the association between PHG and *lncRNA DANCR* expression level in cancer.

Abbreviations: *lncRNA DANCR*, long non-coding RNA anti-differentiation noncoding RNA; PHG, poor histological grade.

lncRNA DANCR has been verified in previous studies to be an important oncogene in various human cancers, including GC, glioma, CVR, OSC, CRC, RB, HCC, and BC.^{22–35} Additionally, *lncRNA DANCR* expression has been confirmed in recent study to be upregulated in CRC tissues, which is correlated with poor survival for CRC patients.^{26,31} Moreover, according to Li et al, *DANCR* could positively promote the proliferation and migration of glioma through activating the Wnt/ β -catenin signaling pathway.²⁴ Besides, Mao et al also

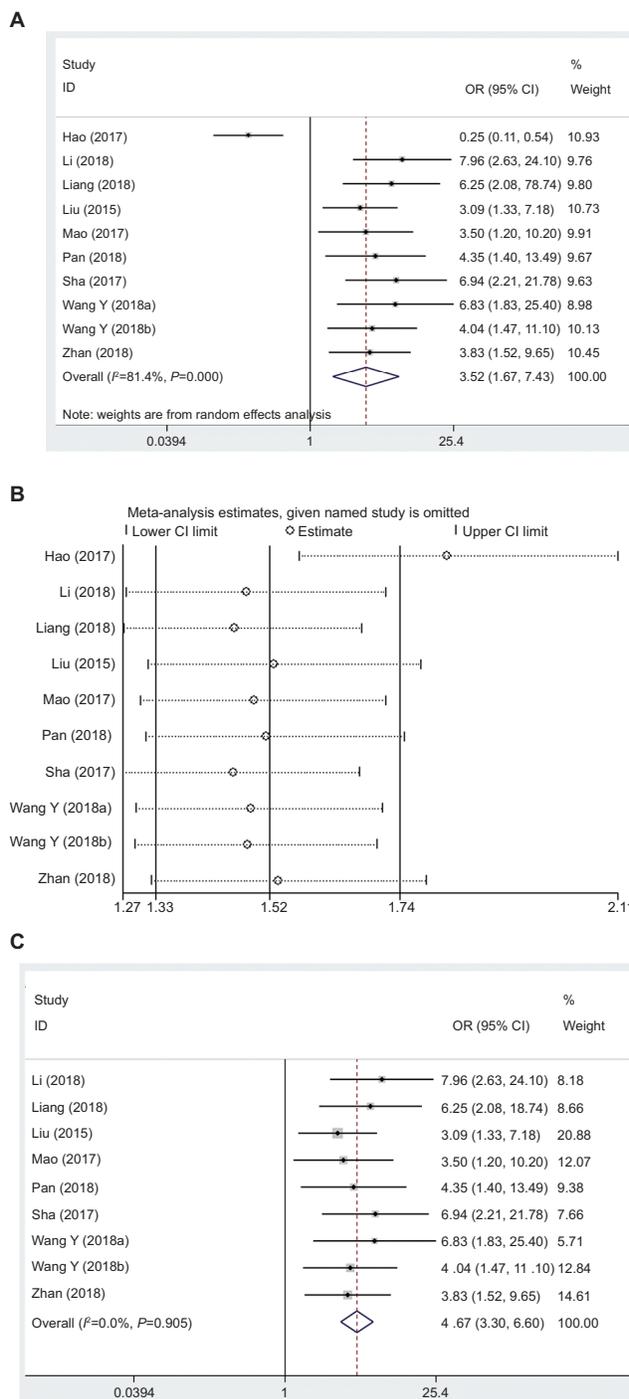


Figure 7 Forest plot (A), sensitivity analysis (B), and the forest plot of sensitivity analysis (C) showed the association between HTS and *lncRNA DANCR* expression level in cancer.

Abbreviations: HTS, high tumor stage; *lncRNA DANCR*, long non-coding RNA anti-differentiation noncoding RNA.

reported that *DANCR* was upregulated in GC tissues, which could enhance the migration and invasion of GC cells.²⁷ Additionally, Wang et al found that *DANCR* could strongly suppress HCC proliferation via targeting miR-216a-5p and KLF12.⁴² Furthermore, Lu et al demonstrated that *DANCR*

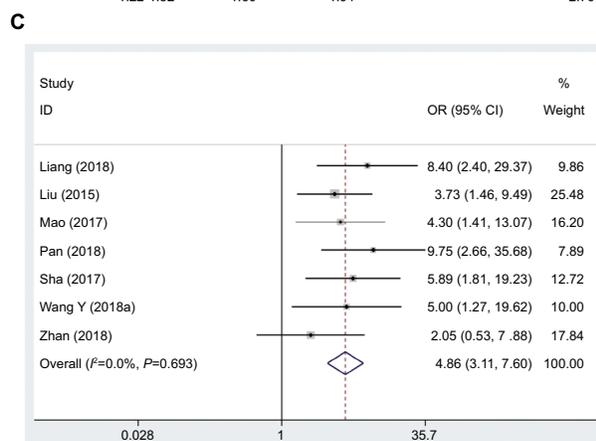
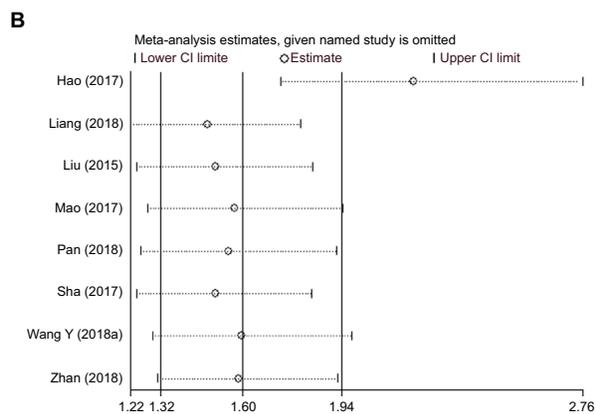
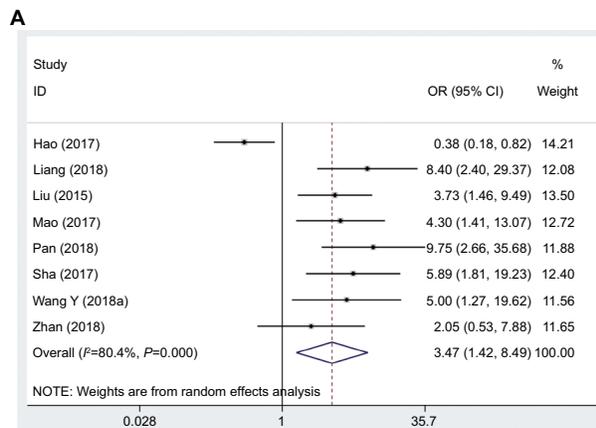


Figure 8 Forest plot (A), sensitivity analysis (B), and the forest plot of sensitivity analysis (C) showed the association between LNM and *lncRNA DANCR* expression level in cancer.

Abbreviations: *lncRNA DANCR*, long non-coding RNA anti-differentiation noncoding RNA; LNM, lymph node metastasis.

was elevated in a broad spectrum of human cancers, and MYC could drive cancer cell proliferation by targeting *DANCR*.⁴³ These results reveal that *lncRNA DANCR* may be a crucial prognostic factor for cancer patients. Nevertheless, the underlying mechanisms by which *lncRNA DANCR* affects cancer remain unknown so far. Therefore, this meta-analysis was performed to examine the prognostic value and clinicopathological significance of *lncRNA DANCR* in cancer patients.

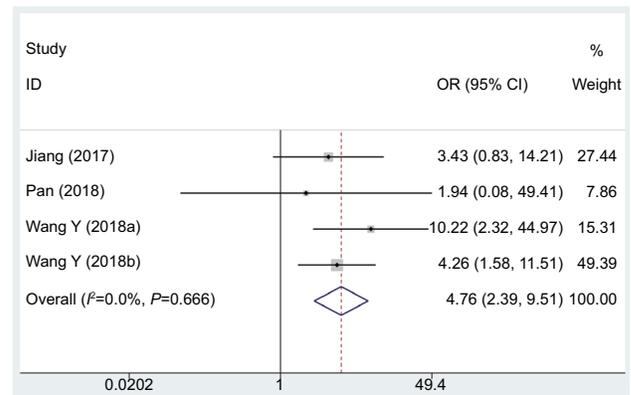


Figure 9 Evaluation of the relationship between *lncRNA DANCR* expression level and DM in cancer.

Abbreviations: DM, distant metastasis; *lncRNA DANCR*, long non-coding RNA anti-differentiation noncoding RNA.

In this research, related data collected from the 14 eligible studies involving 1,117 cancer patients were analyzed, and a fixed or a random effects model had been adopted based on the heterogeneity analysis results. For cancer patients, high *lncRNA DANCR* expression could potentially serve as an indicator of poor prognosis. Besides, significant differences were found in OS and DFS between the two groups after combining HRs from the Cox multivariate analyses, and it was found that poor OS and DFS in various cancer kinds were associated with high *lncRNA DANCR* expression. Moreover, high *lncRNA DANCR* expression in cancer patients was also remarkably related to some clinicopathological parameters, including PHG, HTS, DM, and LNM. To sum up, findings of this meta-analysis indicated that *lncRNA DANCR* might serve as a valuable biomarker for the poor prognosis of most cancers.

Limitations

Several limitations should be taken into consideration when interpreting the conclusion of this meta-analysis. First, data in this meta-analysis might not be applicable for countries all over the world, since all the included studies were from China. Second, in spite of the best effort made to search for all relevant studies only 14 studies were ultimately enrolled in this study; the relatively small sample size might reduce the stringency of our conclusion. Third, the criterion of high expression was not consistent among all articles, making it difficult to obtain the same value. Last but not least, there were other factors that might affect cancer prognosis, such as comorbidities and therapies, but related information was not available in the analyzed enrolled articles, which had therefore become an inherent shortcoming of this systematic review and meta-analysis. As a consequence, the role of

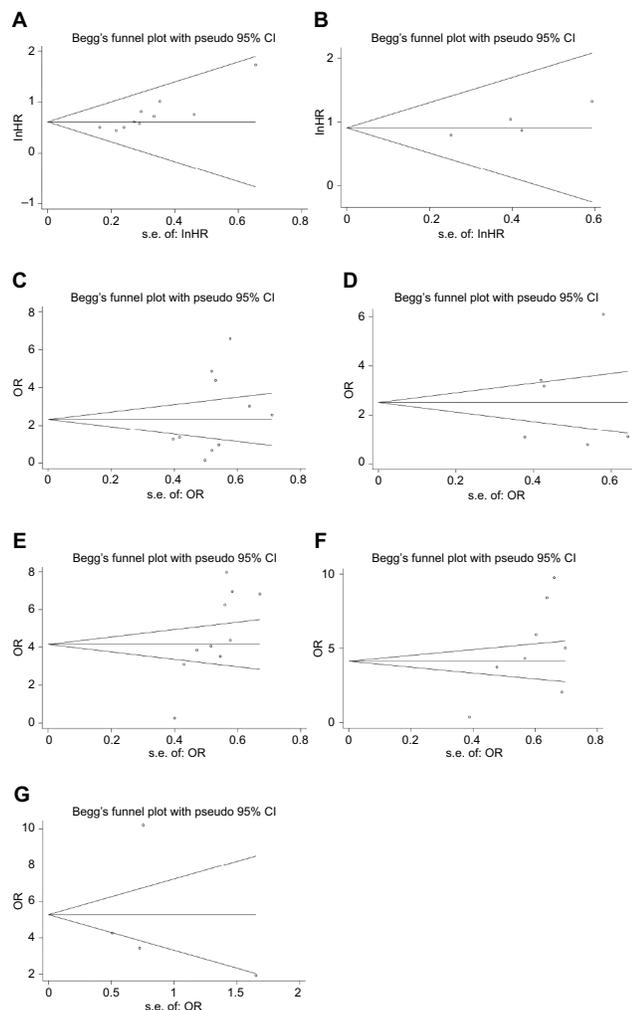


Figure 10 Begg's publication bias plots evaluating the relationship between *lncRNA DANCR* expression and OS (A), DFS (B), LTS (C), PHG (D), HTS (E), LNM (F), DM (G).

Abbreviations: DFS, disease-free survival; DM, distant metastasis; HTS, high tumor stage; *lncRNA DANCR*, long non-coding RNA anti-differentiation noncoding RNA; LNM, lymph node metastasis; LTS, larger tumor size; OS, overall survival; PHG, poor histological grade.

lncRNA DANCR in cancer should be further confirmed by more high-quality and well-designed studies.

Conclusion

To sum up, our findings suggest that high *lncRNA DANCR* expression in a series of cancers is remarkably correlated with poor OS, DFS, PHG, HTS, DM, and LNM. As a result, *lncRNA DANCR* may potentially serve as a biomarker to determine metastasis and predict the prognosis for cancer patients.

Abbreviations

BC, bladder cancer; CRC, colorectal cancer; CVR, cervical cancer; DFS, disease-free survival; DM, distant metastasis; *GAPDH*, glyceraldehyde-3-phosphate dehydrogenase; GC,

gastric cancer; HCC, hepatocellular carcinoma; HTS, high tumor stage; *lncRNA DANCR*, long non-coding RNA anti-differentiation noncoding RNA; LNM, lymph node metastasis; LTS, larger tumor size; NOS, Newcastle–Ottawa Scale; OS, overall survival; OSC, osteosarcoma; PHG, poor histological grade; RB, retinoblastoma; TNBC triple negative breast cancer.

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Disclosure

The authors report no conflicts of interest in this work.

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