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Research Paper

Abnormally expressed long non-coding RNAs in prognosis of Osteosarcoma: A systematic review and meta-analysis

Chen Delong[a,b,1], Wang Haibin[b,c,d,1], Zhang Meng[a,b], Jiang Shan[a,b], Zhou Chi[b,c], Fang Bin[b,c,d], Chen Peng[b,c,d,*]

[a] First Clinical Medicine School, Guangzhou University of Chinese Medicine, 12 Jichang Road, Baiyun Area, Guangzhou 510405, China
[b] Laboratory of Orthopaedic and Traumatology of Chinese Medicine of Lingnan Medical Research Center, Guangzhou University of Chinese Medicine, 12 Jichang Road, Baiyun Area, Guangzhou 510405, China
[c] Orthopedics Department, First Affiliated Hospital of Guangzhou University of Chinese Medicine, 16 Jichang Road, Baiyun Area, Guangzhou 510405, China
[d] Hip Center, Guangzhou University of Chinese Medicine, 16 Jichang Road, Baiyun Area, Guangzhou 510405, China

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ABSTRACT

Background: Numerous studies have reported the relationship between Long non-coding RNAs (LncRNAs) expression and prognosis of osteosarcoma, but less consensus has been reached. Our meta-analysis was conducted to quantitatively assess the relationship between the expression of LncRNAs, prognosis and clinical pathology in osteosarcoma development.

Methods: PubMed,Embase,Web of Science,The Cochrane Library,SionMed,CNKI and WanFang databases were carefully searched to identify eligible studies. The pooled hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated to evaluate the prognostic significance of LncRNAs expression in osteosarcoma. Moreover, meta-regression analysis and subgroup analysis were carried out to explore the potential sources of heterogeneity.

Results: A total of 20 studies comprising 1749 patients were included in present meta-analysis. The results showed that the over-expression of LncRNA had a significant correlation with overall survival (OS) (HR = 2.16, 95% CI:1.68–2.79), and was not related to disease free survival (DFS) (HR = 0.71, 95% CI:0.05–9.53). Subgroup analysis further indicated that LncRNA transcription level was significantly associated with alkaline phosphatase (HR = 2.13, 95% CI:1.58–2.88) , tumor size (< 8/ ≥ 8:HR = 1.97, 95% CI: 1.55–2.62) , metastasis (yes/no: HR = 2.14,95% CI:1.15–3.97) , distant metastasis(presence/absence: HR = 4.02, 95% CI:3.05–5.23) and Enneking stage(IIA /IIB-III:HR = 3.2, 95% CI:2.48–4.14), but not associated with age (≤ 25/ > 25:HR = 1.01, 95% CI:0.78–1.3), gender(female/male: HR = 1.15, 95% CI: 0.96–1.37), tumor site (femur,tibia/elsewhere:HR = 1.15, 95% CI:0.94–1.4) and chemotherapy (yes/no: HR = 1.45, 95% CI:0.46–4.63).

Conclusions: This study demonstrated that abnormal LncRNAs expression might be potential prognostic markers to predict worse overall survival in osteosarcoma patients. However, the cut-off values may be the source of heterogeneity.

1. Introduction

Osteosarcoma (OS) is a highly malignant tumor of bone in children and adolescents [1], which accounts for about 2.4% of malignant tumors in children, and the incidence of OS is about 1–5 cases per million people per year [2,3]. Most patients are diagnosed as OS under the age of 25 years, and there are more men than women among the OS patients [4,5]. Both the metastasis and mortality rates of OS are high in clinic practice. About 20% OS patients were diagnosed with lung metastases at the time of the first diagnosis, and 80% OS metastases occur in the lung [6]. At present, the treatment of OS is mainly based on the combination of surgical resection and multiple chemotherapeutic drugs [7]. The average treatment rate of OS was 65% [8]. The average five-year survival rate of OS patients without metastasis was about 80% [9,10]. 90% OS patients died of recurrence or metastasis due to the presence of tumor resistance, drug side effects and other causes, and the five-year survival rate of OS patients was only 20–30% [11–13]. So far, the molecular mechanism of OS remains unclear. Therefore, finding

* Corresponding author at: Orthopedics Department, First Affiliated Hospital of Guangzhou University of Chinese Medicine, 16 Jichang Road, Baiyun Area, Guangzhou 510405, China.
E-mail address: docchen777@gmail.com (P. Chen).
[1] Both the authors contributed equally to this work.

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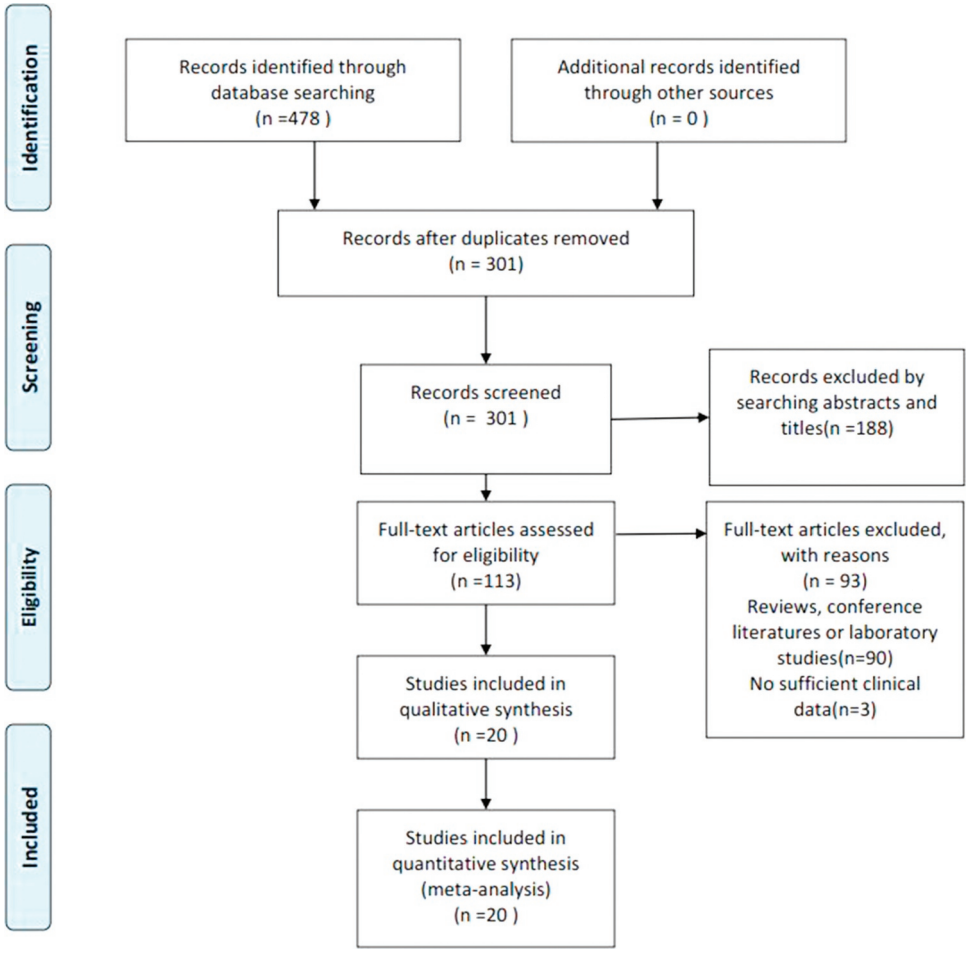

Fig. 1. Flow diagram of study selection process.

Table 1
Comparison of *p* values of relationships between lncRNAs and clinicopathological features in osteosarcoma.

Author	Year	LncRNAs	Country	Case number	Cut-off	Expression	Gender	Age	Tumor site	Tumor size	Tumor stage	Metastasis	ALP	Chemotherapy
Jiang	2017	DANCR	China	34	NA	up-regulated	NA	NA	NA	<0.05	NA	<0.05	NA	NA
Wen	2017	UCA1	China	151	NA	up-regulated	0.572	0.199	0.804	0.907	0.001	0.007	NA	NA
Cai	2017	HNF1A-AS1	China	72	median	up-regulated	0.215	0.534	0.143	0.311	0.019	0.009	0.128	0.031
O'Leary	2017	PARTICLE	Germany	40	NA	up-regulated	0.030	NA	NA	NA	NA	0.01	NA	NA
Huo	2017	MALAT1	China	46	median	up-regulated	0.759	0.473	NA	0.008	0.058	0.000	NA	NA
Li	2017	XIST	China	145	NA	up-regulated	0.827	0.102	0.886	0.009	0.001	0.009	0.704	NA
Wang	2017	SOX2-OT	China	138	median	up-regulated	0.723	0.115	0.191	0.036	0.008	0.001	NA	NA
Zhou	2016	CCAL	China	46	median	up-regulated	0.555	0.200	0.502	0.134	0.017	0.006	NA	NA
Peng	2016	BANCR	China	84	median	up-regulated	0.509	0.505	0.814	0.008	0.004	0.020	0.366	NA
Ju	2016	BCAR4	China	168	median	up-regulated	0.381	0.494	0.982	0.810	0.002	0.001	0.191	0.841
Chen	2016	BCAR4	China	60	median	up-regulated	0.795	0.436	0.754	0.037	0.041	0.028	NA	NA
Ma	2016	TUG1	China	76	fold-change	up-regulated	0.835	0.701	0.093	0.011	0.002	0.802	0.235	0.020
Gao	2016	MALAT1	China	162	median	up-regulated	0.335	0.202	0.193	0.344	0.000	0.001	NA	NA
Cong	2016	TUSC7	China	82	fold-change	dowm-regulated	0.65	0.473	0.627	NA	0.294	0.087	NA	NA
Uzan	2016	HULC	Brazil	33	ROC	up-regulated	0.999	0.065	0.274	0.67	NA	0.999	NA	NA
Xia	2016	91H	China	67	median	up-regulated	0.497	0.927	0.114	<0.001	0.015	0.936	NA	0.023
Li	2016	UCA1	China	135	median	up-regulated	0.573	0.339	0.512	0.005	<0.001	0.002	NA	NA
Tian	2015	MEG3	China	64	median	dowm-regulated	0.614	0.302	0.281	0.076	0.006	0.011	NA	NA
Li	2015	HOTTIP	China	68	median	up-regulated	0.465	0.215	0.161	0.120	0.003	0.016	NA	NA
Sun	2015	HULC	China	78	median	up-regulated	0.492	0.352	0.624	0.496	0.003	0.005	NA	NA

Notes: LncRNA, long non-coding RNA;ALP, alkaline phosphatase;NA, not available.

new molecular markers for early diagnosis and prognosis and therapeutic targets of OS is very important for improving the survival rate of OS patients. Encouragingly, some LncRNAs have recently been reported to play a key role in OS pathogenesis.

LncRNA is a class of non-coding RNAs that are longer than 200 nucleotides in length, with little or no protein coding capacity [14].