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Meta-analysis

Long non-codingRNA (lncRNA) TUG1 and the prognosis of cancer: a meta-analysis

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Abstract: Some studies assessed the association between lncRNA taurine-upregulated gene 1 (TUG1) and the survival in cancer. However, the results were inconclusive. Therefore, we performed a meta-analysis to determine this association. We used the following electronic databases to search for eligible literature: PubMed, Embase, Chinese National Knowledge Infrastructure (CNKI) and Wanfang. We used ORs and 95% CIs to measure the association between TUG1 and the survival of cancer. There was no significant association between TUG1 and OS of cancer (HR=1.26, 95% CI=0.97-1.64). In the subgroup analysis by cancer type, significant association could be find in osteosarcoma (HR=1.72, 95% CI=1.27-2.32) and digestive system's tumors (HR=1.66, 95% CI=1.04-2.66). In conclusion, this meta-analysis study indicated that TUG1 might associate with the OS of osteosarcoma and digestive system's tumors.

Key words: TUG1; Cancer; Association.

Introduction

Cancer is a disease, which can destroy normal tissues and organs. According to the World Health Organization, the most frequent types of cancers causing death include lung, stomach, liver, colon, and breast cancers. Although many technologies have been made, the cancer-related deaths are still high.

Long non-codingRNAs (lncRNAs) are most commonly defined as a non-protein-coding RNA molecule longer than 200 nucleotides (1). Recent studies suggested that lncRNAs played key roles in cancer. Li et al. found that lncRNA NEAT1 could be a new diagnostic biomarker and therapy target for breast cancer (2). Du et al. suggested that PVT1 promotes tumor progression by interacting with FOXM1(3). Liu et al. suggested a regulatory relationship between lncRNA PVT1 and miR-146a during the process of the prostate cancer tumorigenesis (4).

Some studies assessed the association between lncRNA taurine-upregulated gene 1 (TUG1) and the survival in cancer. However, the results were inconclusive(5-12). Therefore, we performed a meta-analysis to determine this association.

Materials and Methods

Literature search

We used the following electronic databases to search for eligible literature: PubMed, Embase, Chinese National Knowledge Infrastructure (CNKI) and Wanfang, and the searching keywords included: “taurine-upregulated gene 1” or “TUG1” and “cancer”. We also searched the references of all eligible studies.

Selection criteria

The studies could be included in the present meta-analysis: (1) assessing the association between TUG1 and the survival of cancer; (2) with a case-control or cohort design; (3) including patients with cancer; and (4) providing sufficient data for calculating hazard ratios (HRs) and 95% confidence intervals (95% CIs). The major reasons for exclusion included: (1) comment, review, or abstract; (2) animal study; and (3) duplicates.

Data extraction

Two authors extracted the data. Any discrepancy was resolved through discussion. The following data were extracted: the first author, publication year, ethnicity, type of cancer, clinical stage, duration of follow-up, samples size, method used to estimate cut-off value, outcome, and covariants.

Statistical analyses

We used ORs and 95% CIs to measure the association between TUG1 and the survival of cancer. We utilized STATA software to carry out all statistical analysis in the meta-analysis. Heterogeneity across studies was examined with the Chi-square-based Q-statistical test. When P value was less than 0.05 in the Q test which indicated significant heterogeneity, the random-effects model was used to calculate the HRs and 95% CIs; otherwise, fixed-effects model was employed. Stratification analyses were also carried out based on can-

cer type. Sequential deletion of included studies was conducted in sensitivity analysis so as to assess the stability of the final results. Begg's funnel plot and Egger's linear regression test were applied to test publication bias. The statistically significant level of all tests was set at P<0.05.

Results

Study characteristics

Eight studies with 967 patients were included in this meta-analysis. Major characteristics of all included studies are shown in Table 1. Most of the studies included Chinese patients. All the studies provided the overall survival (OS) data. Five studies provided the covariants data.

Meta-analysis results

As demonstrated in Figure 1, there was no significant association between TUG1 and OS of cancer (HR=1.26, 95% CI=0.97-1.64). In the subgroup analysis by cancer type, significant association could be find in osteosarcoma (HR=1.72, 95% CI=1.27-2.32) and digestive system's tumors (HR=1.66, 95% CI=1.04-2.66). The results are shown in Table 2.

Publication bias

We used Begg's funnel plots and Egger's test to evaluate publication bias. No apparent asymmetry was revealed in funnel plot (Figure 2). Egger's test was also no significant.

Discussion

Long et al. indicated that a direct interaction between PGC-1α and Tug1 modulates mitochondrial bioenergetics in podocytes in the diabetic milieu(13). Zhai et al. found that overexpressed TUG1 may contribute to promoting cell proliferation and migration in colon cancer cells. (14) Xie et al. elucidated a novel TUG1/miR-9-5p/POU2F1 pathway leading to downregulation of POU2F1 and facilitating the tumorigenesis of osteosarcoma(15). Chen et al. suggested that low TUG1 expression and high level of miR-26a are associated with the endothelial protecting effect of tanshinol(16). Zhao et al. indicated that TUG1 knockdown was significantly associated with decreasing cell proliferation and promoting cell apoptosis in breast cancer cells(17).

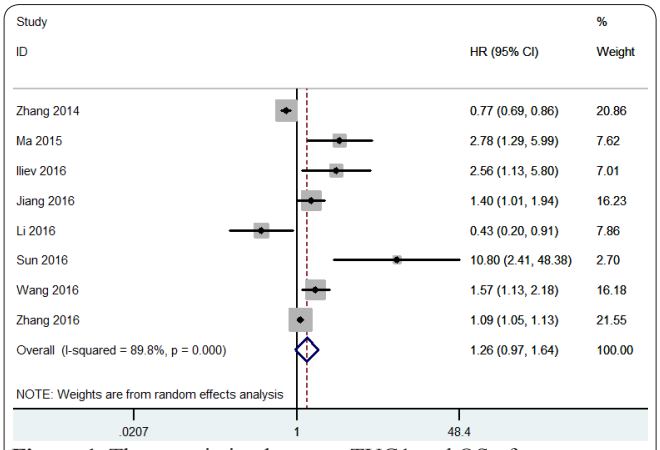

Figure 1. The association between TUG1 and OS of cancer.

Table 2. Results of this meta-analysis.

	HR (95% CI)	*P* Value	I^2 (%)
Overall survival	1.26 (0.97-1.64)	0.08	90
Site of cancer			
Osteosarcoma	1.72 (1.27-2.32)	0.0005	44
Digestive cancer	1.66 (1.04-2.66)	0.03	80

In this meta-analysis, we included eight studies with 967 patients. There was no significant association between TUG1 and OS of cancer. In the subgroup analysis by cancer type, significant association could be find in osteosarcoma and digestive system's tumors.

Some limitations should be noted. First, the sample sizes of included studies were small. Second, the possibility of publication bias cannot be ruled. Third, a lack of original data from the eligible studies limited evaluation of the effects of other clinical factors.

In conclusion, this meta-analysis study indicated that TUG1 might associate with the OS of osteosarcoma and digestive system's tumors.

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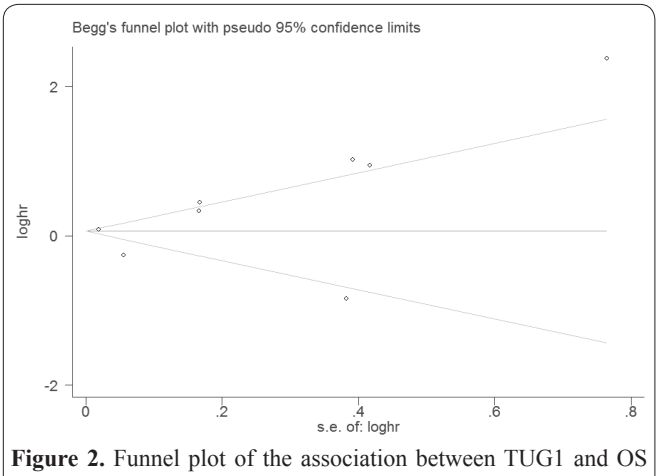

Figure 2. Funnel plot of the association between TUG1 and OS of cancer.

Table 1. Characteristics of the included studies.

First author	Year	Ethnicity	Cancer type	Clinical stage	Follow-up (month)	Samle size	Method used to detect UCA1	Reference gene	Method used to estimate cut-off value	Outcome	Covariants use in survival analysis
Zhang	2014	Chinese	NSCLC	I-IV	60	192	Real-time PCR	GAPDH	$2^{-\Delta\Delta CT}$	OS	Histological grade, tumor stage
Ma	2015	Chinese	Osteosarcoma	I-III	60	76	Real-time PCR	β-actin	ROC analysis	OS, PFS	Alkaline phosphatase, tumor stage, chemotherapy, initial metastasis
Iliev	2016	Caucasian	Bladder cancer	I-IV	30	47	Real-time PCR	RNU48	$2^{-\Delta\Delta CT}$	OS	NA
Jiang	2016	Chinese	ESCC	I-IV	12-72	218	Real-time PCR	GAPDH	$2^{-\Delta\Delta CT}$	OS	Lymph node metastasis, tumor stage
Li	2016	Chinese	Glioma	I-IV	NA	120	Real-time PCR	GAPDH	$2^{-\Delta\Delta CT}$	OS	NA
Sun	2016	Chinese	Colorectal cancer	NA	36	120	Real-time PCR	GAPDH	$2^{-\Delta\Delta CT}$	OS	NA
Wang	2016	Chinese	Osteosarcoma	IIA-III	32	94	Real-time PCR	β-actin	$2^{-\Delta\Delta CT}$	OS	Tumor stage
Zhang	2016	Chinese	Gastric cancer	I-IV	NA	100	Real-time PCR	β-actin	$2^{-\Delta\Delta CT}$	OS	Lymph node metastasis, tumor stage, distant metastasis

GAPDH, glyceraldehyde-3-phosphate dehydrogenase; CT, cycle threshold; ESCC, esophageal squamous cell carcinoma; NSCLC, non-small cell lung cancer; OS, overall survival; PFS, progression-free survival; NA, not available.

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