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Clinicopathologic and prognostic significance of long non-coding RNA myocardial infarction-associated transcript in multiple cancers

Y.-P. ZHANG[1], Y.-W. LI[1], Y.-L. DAI[1], J. ZHOU[2], Z.-M. TU[1], B. JIANG[1], B. WANG[1]

[1]Department of Spine Surgery, [2]Department of Orthopedics, The Second Xiangya Hospital of Central South University, Changsha, Hunan, China

Abstract. – OBJECTIVE: The aim of the meta-analysis was to explore the clinicopathological and prognostic significance of long non-coding RNA (lncRNA) myocardial infarction-associated transcript (MIAT) in various cancers.

MATERIALS AND METHODS: We searched multiple databases, including PubMed, China National Knowledge 53 Infrastructure (CNKI), Springer, Web of Science, and Cochrane, for articles on the prognostic value of lncRNA MIAT in various cancers before 25 March 2021. The odds ratio (OR) and 95% confidence interval (CI) were adopted to evaluate the clinicopathological features and outcomes of cancers. The Cancer Genome Atlas dataset was used to identify the differential expression and prognostic significance of lncRNA MIAT.

RESULTS: We enrolled 14 publications, including 1,573 cancer patients. Higher lncRNA MIAT expression was significantly related to worse overall survival (OR=3.13, 95% CI: 2.47-3.96, $p<0.05$), regardless of cancer types, sample size, and follow-up time of the included studies. Additionally, higher lncRNA MIAT expression was associated with larger tumour sizes (OR=1.67, 95% CI: 1.24-2.26, $p<0.05$), advanced clinical stage (OR=4.79, 95% CI: 3.38-6.79, $p<0.05$), lymph nodes metastasis (OR=7.33, 95% CI: 4.61-11.67, $p<0.05$), and distant metastasis (OR=2.62, 95% CI: 1.88-3.66, $p<0.05$), but not associated with age and gender. We found no publication bias, and sensitivity analysis indicated that the results were reliable.

CONCLUSIONS: Higher lncRNA MIAT expression may predict larger tumour sizes, advanced clinical stage, metastasis of cancers, and lower overall survival rate. LncRNA MIAT may serve as a useful clinicopathological and prognostic biomarker for cancers.

Key Words:
LncRNA MIAT, Clinicopathological features, Prognosis, Meta-analysis, TCGA dataset.

Abbreviations

Acute myeloid leukemia (AML); Brain lower grade glioma (LGG); China National Knowledge Infrastructure (CNKI); Disease-free survival (DFS); Glioblastoma multiforme (GBM); Head and neck squamous cell carcinoma (HNSC); Kidney chromophobe (KICH); Kidney renal clear cell carcinoma (KIRC); Lung adenocarcinoma (LUAD); Lymphoid neoplasm diffuse large B-cell lymphoma (DLBC); LncRNA MIAT (lncMIAT); Newcastle-Ottawa Scale (NOS); Odds ratio (OR); Overall survival (OS); Ovarian serous cystadenocarcinoma (OV); Prostate adenocarcinoma (PRAD); Pheochromocytoma and paraganglioma (PCPG); Quantitative real-time polymerase chain reaction (qRT-PCR); Rectum adenocarcinoma (READ); Skin cutaneous melanoma (SKCM); The Cancer Genome Atlas (TCGA); Testicular germ cell tumors (TGCT); Thymoma (THYM); Uveal melanoma (UVM); 95% confidence interval (95% CI)

Introduction

Cancer is a leading cause of death worldwide, with a continuous rise in its incidence and prevalence. In 2019, more than 1,762,450 new cancer cases and 606,880 cancer deaths reportedly occurred in the United States[1]. Malignant tumours devastatingly reduce humans' quality of life and longevity, and patients' clinical prognosis after cancer treatment is frequently poor. Hence, strategies that facilitate early identification, diagnosis, and consequently, timely treatment of cancer will have considerable clinical significance in improving the survival rates of cancer patients[2]. By far, many traditional markers have been used in clinical practice to help diagnose various tumours and monitor tumour recurrence after treatment[3,4]. However, the specificity and sensitivity of these markers for diagnosing cancers and monitoring recurrent events are often unsatisfactory. Hence, new biomarkers with high specificity and sensitivity will be useful to improve this issue[5-7].

Corresponding Author: Bing Wang, MD; e-mail: wbxyeyy@csu.edu.cn

Long non-coding RNA (lncRNA) is a non-coding RNA with >200 nucleotides. As a regulatory molecule, it plays a role in various tumours through complex mechanisms[8]. Moreover, previous scholars[9] have shown that specific lncRNA was related to cancer development and can be detected in tissues. Thus, lncRNA has the potential to serve as a useful biomarker for tumour detection, diagnosis, grading, and monitoring of recurrent events.

Robust evidence[10-12] has shown that lncRNA MIAT, a newly discovered lncRNA, is abnormally expressed in various tumour cells. The level of lncRNA MIAT expression was closely related to the degree of malignancy. Xu et al[13] found that lncRNA MIAT may serve as a promising biomarker for monitoring the progression of gastric cancers. Additionally, Zhou et al[14] found that lncRNA MIAT could serve as a potential biomarker and therapeutic target for the management of non-small cell lung cancers. Evidence suggests that lncRNA may have an important prognostic value for cancers. Herein, we conducted a meta-analysis of currently available studies to assess the association between the lncRNA MIAT expression and the prognosis of multiple cancers.

Materials and Methods

Search Strategy

PubMed, CNKI, Springer, Web of Science, and Cochrane were searched for studies published before 25 September 2021 on lncRNA MIAT and cancer. The following terms: ("long non-coding RNA" or "lncRNA"), ("myocardial infarction association transcript" or "MIAT"), ("cancer", "tumour", "carcinoma", or "sarcoma"), and ("metastasis", "prognosis", "5-year survival", or "clinical outcome") were used for this search, which was conducted by two researchers, JZ and WW, respectively. **PRISMA guidelines** were followed to conduct the search.

Inclusion and Exclusion Criteria

The inclusion criteria were: (1) Publications with data that could be used to derive the odds ratio (OR) and 95% confidence interval (CI) or with ready-for-use data. (2) Studies that assessed the clinicopathological or prognostic significance of lncRNA MIAT in human cancers. (3) Studies that categorised patients according to high or low lncRNA MIAT expression. (4) Articles published from 2017 and onward. (5) Case-control studies.

The exclusion criteria were: (1) Studies without provided survival outcomes, (2) studies that were not original research, (3) repeated publications, and (4) studies without association.

Data Extraction

Two authors (JZ and WW) extracted the relevant data according to the exclusion and inclusion criteria, including (1) the name of the first author, (2) publication year, (3) study design, (4) country where the study participants were recruited, (5) type of sample used in the article, (6) tumour type, (7) the number of cases, (8) number of patients with high/low (H/L) for lncRNA MIAT expression, (9) gender, (10) inclusion period, (11) follow-up time, and (12) method of cancer detection. After that, the full texts were independently checked. An additional author (YL) resolved differences in the data collected between the two authors. If any further data was needed, we contacted the study's corresponding author by e-mail, and the article was excluded if no response was received. Our previous studies described the study selection and extraction process in detail[3,15,16].

Assessment of Included Studies

The most commonly used tool for assessing the quality of case-control studies in a meta-analysis is the Newcastle-Ottawa Scale (NOS)[17]. Hence, we applied the NOS assessment in this meta-analysis. The scale uses stars to represent the score, with a total score of nine stars. The NOS has three groups of evaluated items: object selection, comparability, and exposure. Each item was evaluated, appropriate items were indicated using a star, and the comparison item could be rated up to two stars. Studies with quality evaluation valued >6 stars were included in this meta-analysis.

Statistical Analysis

All data were statistically analysed using Stata 12.0 and Excel 2007. We evaluated the between-study heterogeneity using I^2 statistics[18], with $p<0.05$ and $I^2>50\%$ denoting statistical significance. We used a fixed-effect model to pool the data if no significant heterogeneity was observed. Otherwise, we pooled data using a random-effect model. The relationship between lncRNA MIAT expression and clinicopathological data or prognosis for cancers was described using the OR and 95% CI. A sensitivity analysis was performed by sequentially omitting individual articles to assess

the stability of the results. Publication bias was detected using Egger's test and Begg's funnel plots[19].

Evaluation of Prognosis Using MIAT in The Cancer Genome Atlas (TCGA) Dataset

TCGA dataset was used to further explore the differential expression patterns of MIAT between normal tissues and cancer tissues for multiple cancers. Moreover, the Kaplan-Meier curve was used to show the association between MIAT and survival, including overall survival (OS) and disease-free survival (DFS) of cancers[20-22].

Results

Search Results

A total of 79 publications were obtained from the first search. We excluded (1) 11 papers because they were duplicate publications, (2) 13 because they had irrelevant topics, and (3) 21 papers because they either had no corresponding topic, were the wrong article type, protocols only, or had other clinical outcomes. After further review, 20 more articles were removed because they had low quality, wrong design or comparison, and lacked usable data. Finally, 14 publications[13,14,23-34] published between 2017 and 2020 were retrieved (Figure 1).

Characteristics for Included Reports and Qualitative Assessment

This meta-analysis included 14 articles including 1573 cancer patients, and all the included studies were retrospective and conducted in China. Tissue/exosomes/serum samples were used for cancer detection. The types of malignant tumours studied in the publications included (1) gastric cancer, (2) hepatocellular carcinoma, (3) non-small cell lung cancer, (4) myeloma, (5) myeloid leukaemia, (6) thyroid cancer, (7) lung cancer, (8) pancreatic carcinoma, (9) clear cell renal cell carcinoma, (10) ovarian cancer, (11) osteosarcoma, and (12) colon cancer. The number of cases in each article ranged from 27-448. The articles detected lncRNA MIAT expression using quantitative real-time polymerase chain reaction (qRT-PCR). Ten studies reported OS, and eleven provided clinicopathological data, including age, gender, tumour size, clinical stage, lymph nodes metastasis, and distant metastasis. The NOS scores of the 14 included studies ranged from 7-8, with an average score of 7.5 (Table I). The detailed quality assessment results are shown in the **Supplementary Table I**.

Association Between LncRNA MIAT Expression and Survival of Cancer Patients

Data from nine articles were pooled to analyse the relationship between lncRNA MIAT expression and patients' survival for various cancers. Using a fixed-effect model (p=0.228, I^2=24.2%), the pooled OR and 95% CI for all-cause mortality for high lncRNA MIAT expression was 3.13 (2.47-3.96) compared to low lncRNA MIAT expression, suggesting that high lncRNA MIAT expression predicted an unfavourable OS (Figure 2, Table II). Additionally, we performed four subgroup analyses by cancer types (gastric cancer, lung cancer, and others), sample size (≥100 and <100), follow-up time (≥60 and <60 months), and survival type (OS, DFS, PFS, and RFS). The results showed that these stratification variables did not moderate the prognostic value of lncRNA MIAT in patients with cancer except for pancreatic carcinoma (Figure 2A-D). The ORs and 95% CIs are presented in Table II. Moreover, sensitivity analysis revealed that our results were stable (Figure 2E), and our main analyses showed no publication bias (Figure 2F).

Association Between LncRNA MIAT Expression and Clinicopathological Features for Cancers

The relationship of lncRNA MIAT expression with six potentially influencing factors, including age, gender, tumour size, clinical stage, lymph nodes metastasis, and distant cancer metastasis, were analysed. The results showed that a high lncRNA MIAT expression was significantly positively associated with tumour size (OR=1.67, 95% CI: 1.24-2.26, p<0.05) (Figure 3C), advanced clinical stage (OR=4.79, 95% CI: 3.38-6.79, p<0.05) regardless of cancer types (Figure 3D), lymph nodes metastasis (OR=7.33, 95% CI: 4.61-11.67, p<0.05) (Figure 3E), and distant metastasis (OR=2.62, 95% CI: 1.88-3.66, p<0.05) (Figure 3F), but not associated with age (Figure 3B) and gender (Figure 3A). The detailed results, including OR, 95% CI, and heterogeneity, are presented in Table III.

When a single article enrolled in this meta-analysis was deleted, we found no significant change in between-study heterogeneity. The

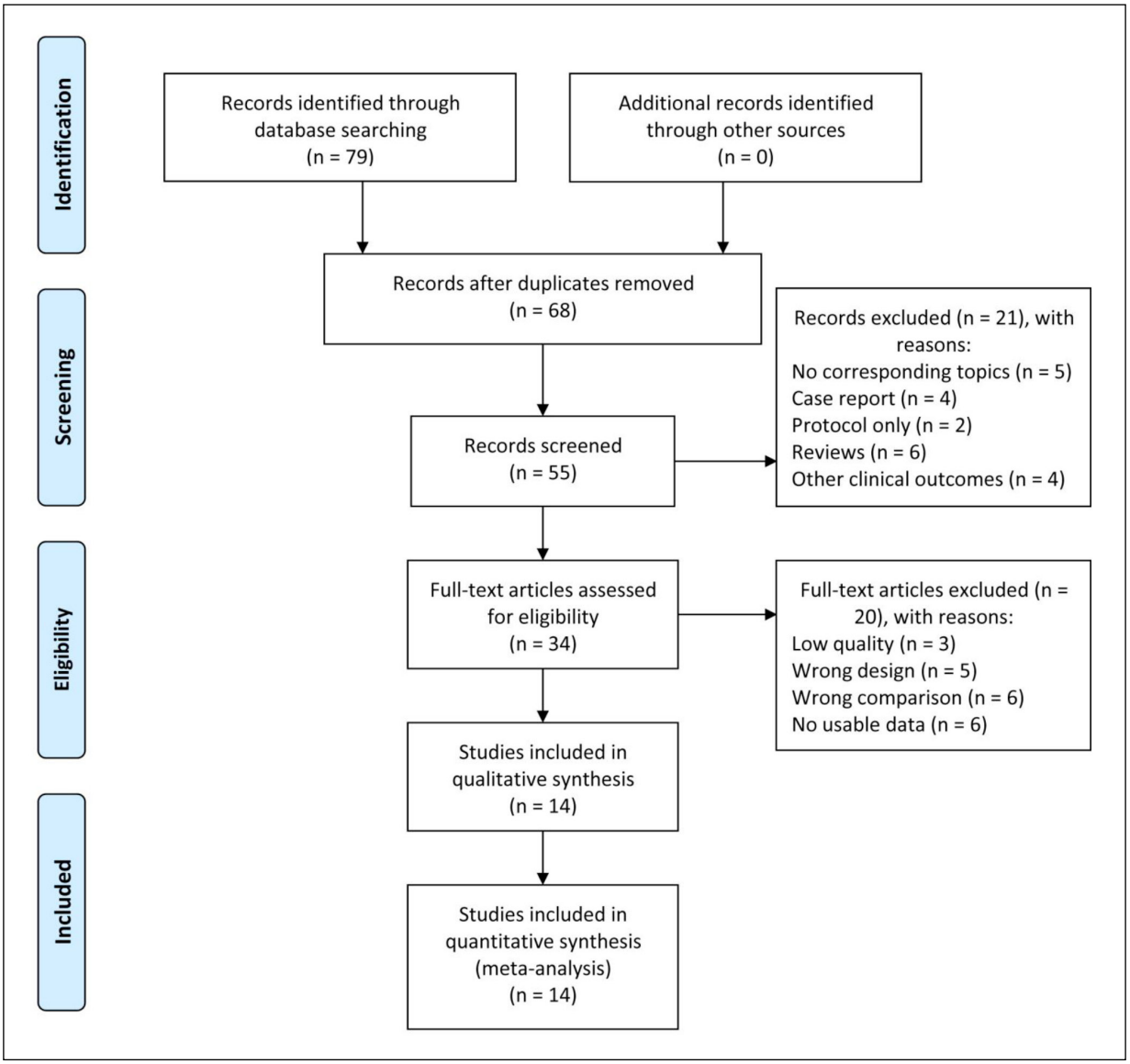

Figure 1. The flow chart for publication screening.

robustness of the obtained results was assessed using a leave-one-out sensitivity analysis; the results indicated that the pooled risk estimates obtained in the main analyses were not dependent on the effect size of the risk estimate in any single paper (Figure 4).

Begg's funnel plot and Egger's test were used to evaluate the potential publication bias. We found no evidence of asymmetry in the funnel plot (Figure 5) and no significant publication bias based on Egger's test ($p>0.05$).

Prognostic Analysis of MIAT in TCGA Dataset

The levels of MIAT expression in multiple cancers were analysed based on the TCGA dataset. MIAT was significantly differentially expressed in lymphoid neoplasm diffuse large B-cell lymphoma, glioblastoma multiforme, acute myeloid leukaemia (LAML), brain lower-grade glioma, lung adenocarcinoma, pheochromocytoma and paraganglioma, testicular germ cell tumours (TGCT), and thymoma (THYM), compared with the controls (Figure 6).

The results from the TCGA dataset showed that higher MIAT expression predicted a worse OS in head and neck squamous cell carcinoma, kidney chromophobe (KICH), kidney renal clear cell carcinoma (KIRC), LAML, rectum adenocarcinoma

Table I. Characteristics of 14 studies for this meta-analysis.

No.	First author	Year	Study design	Country	Type of sample	Tumor type	Cases	LncMIAT (H/L)	Gender (M/F)	Inclusion period	Follow up (month)	Method	Chemistry	NOS score
1	Xu et al[13]	2020	Retrospective	China	Exosomes	Gastric cancer	109	54/55	81/28	-	60	qRT-PCR	SYBR Green	7
2	Yang et al[23]	2020	Retrospective	China	Serum	Hepatocellular carcinoma	40	20/20	35/5	-	-	qRT-PCR	SYBR Green	8
3	Zhou et al[14]	2020	Retrospective	China	Tissue	Non-small cell lung cancer	80	40/40	-	-	60	qRT-PCR	SYBR Green	8
4	Fu et al[24]	2019	Retrospective	China	Tissue	Myeloma	123	85/38	72/51	-	60	qRT-PCR	SYBR Green	8
5	Li et al[25]	2019	Retrospective	China	Tissue	Gastric cancer	92	49/43	51/41	2008-2013	60	qRT-PCR	NA	7
6	Wang et al[26]	2019	Retrospective	China	Tissue	Acute myeloid leukemia	121	61/60	64/57	-	60	qRT-PCR	SYBR Green	7
7	Wang et al[27]	2019	Retrospective	China	Tissue	Thyroid cancer	50	28/22	18/32	-	-	qRT-PCR	SYBR Green	8
8	Fu et al[28]	2018	Retrospective	China	Tissue	Lung cancer	212	129/83	134/78	2011-2011	60	qRT-PCR	SYBR Green	7
9	Li et al[29]	2019	Retrospective	China	Tissue	Pancreatic carcinoma	38	20/18	-	-	24	qRT-PCR	SYBR Green	7
10	Qu et al[30]	2018	Retrospective	China	Tissue	Clear Cell Renal Cell Carcinoma	448	224/224	287/161	2010-2016	120	qRT-PCR	SYBR Green	7
11	Sha et al[31]	2018	Retrospective	China	Tissue	Gastric cancer	120	65/55	70/50	2014-2016	-	qRT-PCR	NA	8
12	Shao et al[32]	2018	Retrospective	China	Tissue	Ovarian cancer	53	27/26	-	2011-2012	60	qRT-PCR	SYBR Green	8
13	Zhang et al[33]	2018	Retrospective	China	Tissue	Osteosarcoma	27	13/14	15/12	2015-2018	-	qRT-PCR	SYBR Green	7
14	Liu et al[34]	2017	Retrospective	China	Tissue	Colon cancer	60	16/44	40/20	2014-2015	24	qRT-PCR	SYBR Green	8

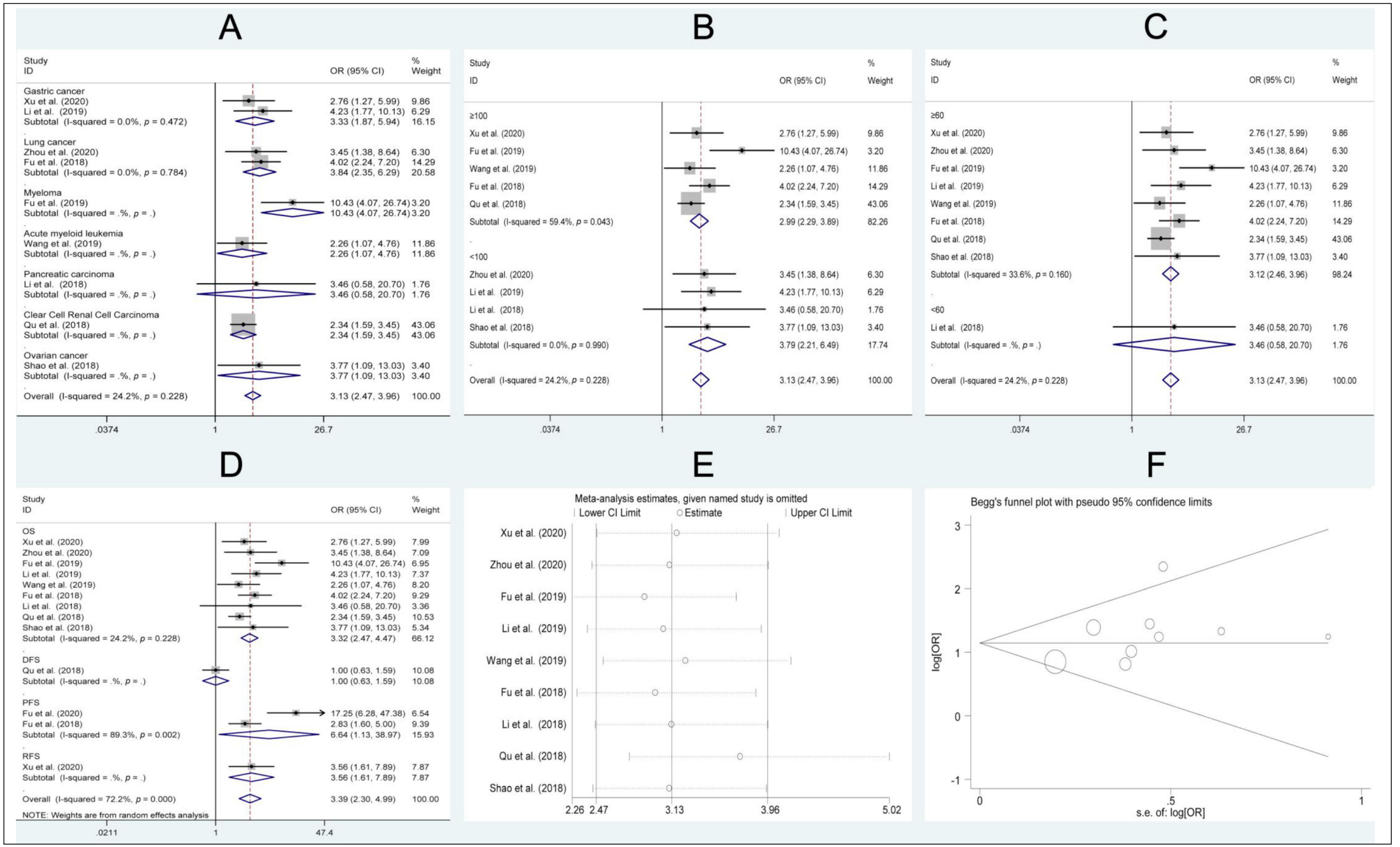

Figure 2. Forest plots for overall and subgroup analysis of association between high expression of lncMIAT and survival of cancers. Subgroup analysis included (**A**) cancer type, (**B**) sample size, (**C**) follow-up months and (**D**) survival outcomes; (**E**) sensitivity analysis; (**F**) publication bias.

Table II. Subgroup analyses for the relationship between high expression of lncMIAT and the survival of patients with cancer.

Subgroup	Studies	OR and 95% CI	Effects model	Heterogeneity (p; I^2)
Cancer types	9	3.13 (2.47-3.96)	Fixed	0.228; 24.2%
Gastric cancer	2	3.33 (1.87-5.94)	Fixed	0.472; 0.0%
Lung cancer	2	3.84 (2.35-6.29)	Fixed	0.784; 0.0%
Meyloma	1	10.43 (4.07-26.74)	-	-
Acute myeloid leukemia	1	2.26 (1.07-4.76)	-	-
Pancreatic carcinoma	1	3.46 (0.58-20.70)	-	-
Clear cell renal cell carcinoma	1	2.34 (1.59-3.45)	-	-
Ovarian cancer	1	3.77 (1.09-13.03)	-	-
Cases	9	3.13 (2.47-3.96)	Fixed	0.228; 24.2%
≥100	5	2.99 (2.29-3.89)	Random	0.043; 59.4%
<100	4	3.79 (2.21-6.49)	Fixed	0.990; 0.0%
Follow-up months	9	3.13 (2.47-3.96)	Fixed	0.228; 24.2%
≥60	8	3.12 (2.46-3.96)	Fixed	0.160; 33.6%
<60	1	3.46 (0.58-20.70)	-	-
Outcomes	13	3.39 (2.30-4.99)	Random	0.000; 72.2%
OS	9	3.32 (2.47-4.47)	Fixed	0.228; 24.2%
DFS	1	1.00 (0.63-1.59)	-	-
PFS	2	6.64 (1.13-38.97)	Random	0.002; 89.3%
RFS	1	3.56 (1.61-7.89)	-	-

(READ), TGCT and THYM (p<0.05) (Figure 7A-G). Furthermore, higher MIAT expression also predicted a worse DFS in KICH, ovarian serous cystadenocarcinoma (OV), prostate adenocarcinoma, skin cutaneous melanoma, and uveal melanoma (UVM) (p<0.05) (Figure 7H-L).

Discussion

LncRNA was once considered to have no biological functions. However, more recent studies[35-38] have found that lncRNA affects various physiological and pathological processes in the body mainly through gene regulation, transcription, mRNA shearing, and translation. However, lncRNA is not involved in protein coding. LncRNA has also been linked closely to tumour proliferation, migration, and invasion ability[38,39].

MIAT, first reported in 2000, is located in region 1 of the long arm of chromosome 22, with a length of 30,051 bp[40]. Ishii et al[41] initially revealed a susceptibility site for myocardial infarction through single nucleotide polymorphism studies. They isolated a complete complementary DNA of a new gene from this site and named it MIAT. Many studies[26,28,30] have reported the prognostic value of lncRNA MIAT in various cancers. Fu et al[28] found that silencing MIAT could inhibit multiple myeloma cell growth by negatively regulating miR-29b.

Table III. Correlation between high expression of lncMIAT and clinicopathologic features for tumor.

Subgroup	Studies	OR and 95% CI	Effects model	Heterogeneity (p; I^2)
Gender	11	0.97 (0.77-1.21)	Fixed	0.991; 0.0%
Age	11	1.13 (0.91-1.40)	Fixed	0.969; 0.0%
<60 *vs.* ≥60	7	1.07 (0.84-1.36)	Fixed	0.954; 0.0%
<50 *vs.* ≥50	3	1.42 0.84-2.38)	Fixed	0.683; 0.0%
<18 *vs.* ≥18	1	1.54 (0.33-7.23)	-	-
Tumor size	8	1.67 (1.24-2.26)	Fixed	0.122; 38.6%
Clinical stage	7	4.79 (3.38-6.79)	Fixed	0.161; 35.0%
Gastric cancer	3	5.87 (3.58-9.60)	Fixed	0.461; 0.0%
Hepatocellular carcinoma	1	19.00 (2.12-170.38)	-	-
Thyroid cancer	1	13.59 (1.59-116.03)	-	-
Lung cancer	1	2.49 (1.35-4.60)	-	-
Colon cancer	1	6.39 (2.07-19.68)	-	-
Lymph node metastasis	5	7.33 (4.61-11.67)	Fixed	0.581; 0.0%
Distant metastasis	6	2.62 (1.88-3.66)	Fixed	0.236; 26.5%

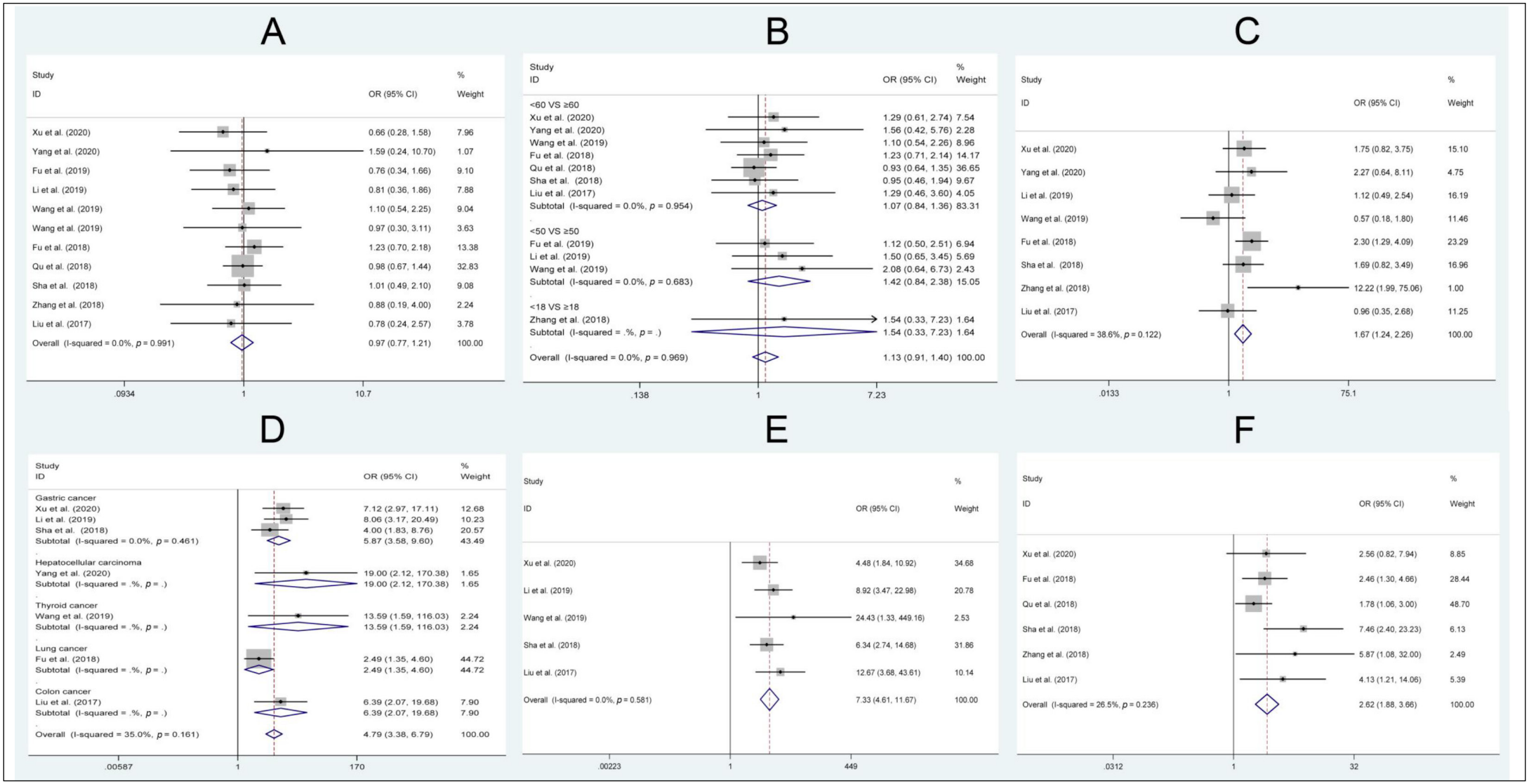

Figure 3. Relationship between high expression of lncMIAT and clinical features of cancers. (**A**) Gender, (**B**) age, (**C**) tumor size, (**D**) clinical stages, (**E**) lymph node metastasis and (**F**) distant metastasis.

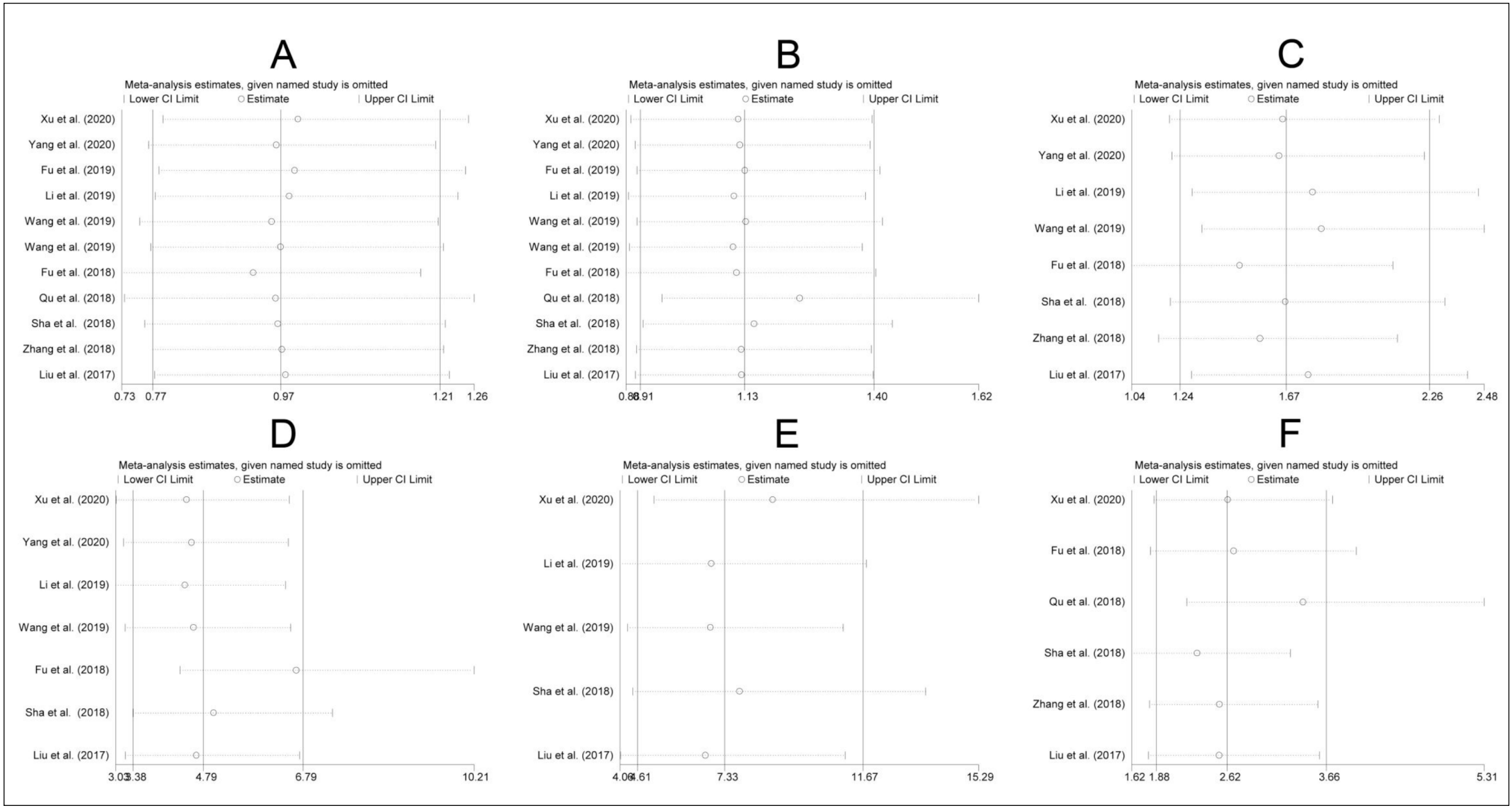

Figure 4. Sensitivity analysis on the relationship for high expression of lncMIAT and clinical features of cancers. (**A**) gender, (**B**) age, (**C**) tumor size, (**D**) clinical stages, (**E**) lymph node metastasis and (**F**) distant metastasis.

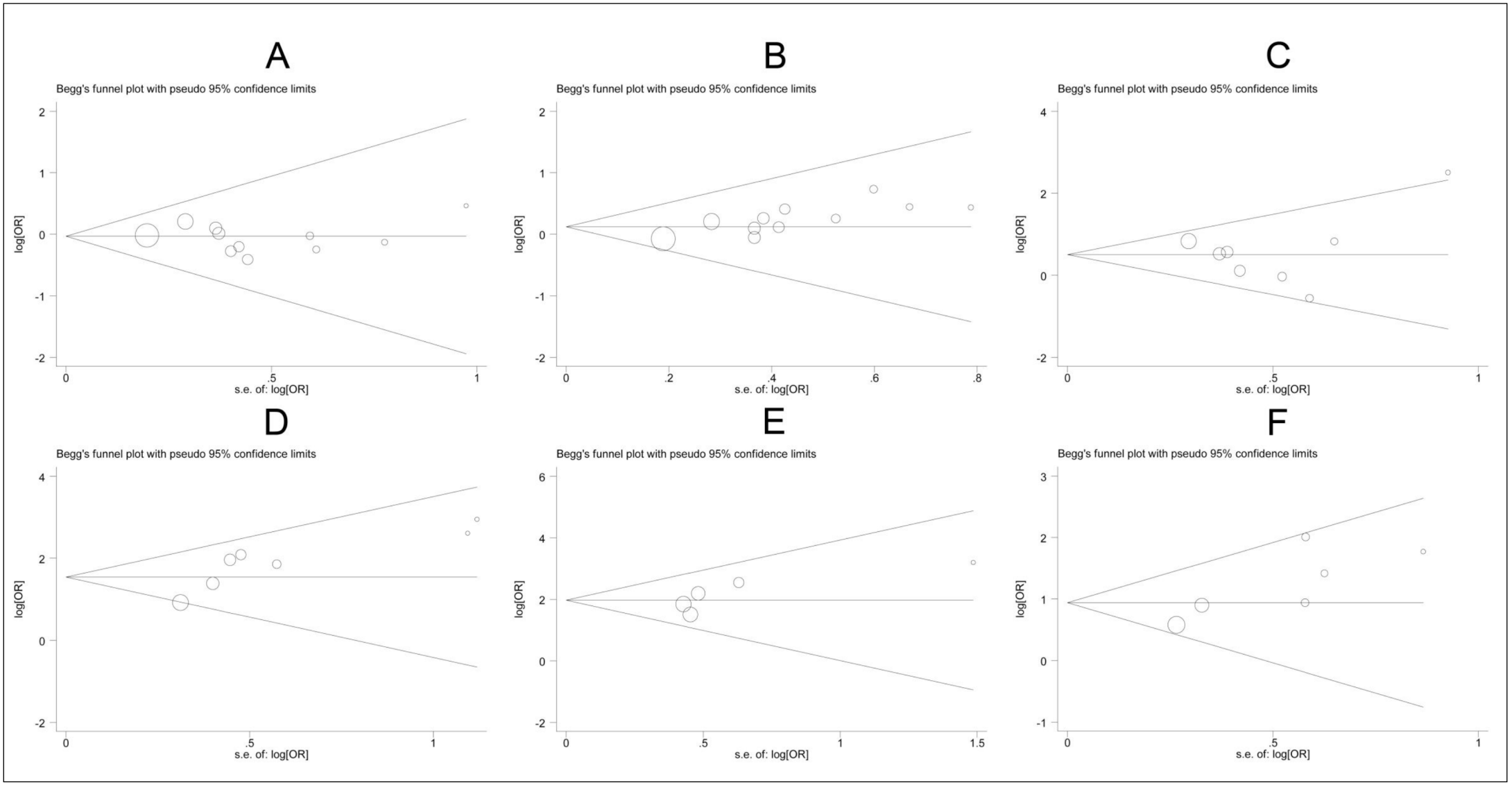

Figure 5. Funnel plot in the meta-analysis of relationship for high expression of lncMIAT and clinical features of cancers. (**A**) gender, (**B**) age, (**C**) tumor size, (**D**) clinical stages, (**E**) lymph node metastasis and (**F**) distant metastasis.

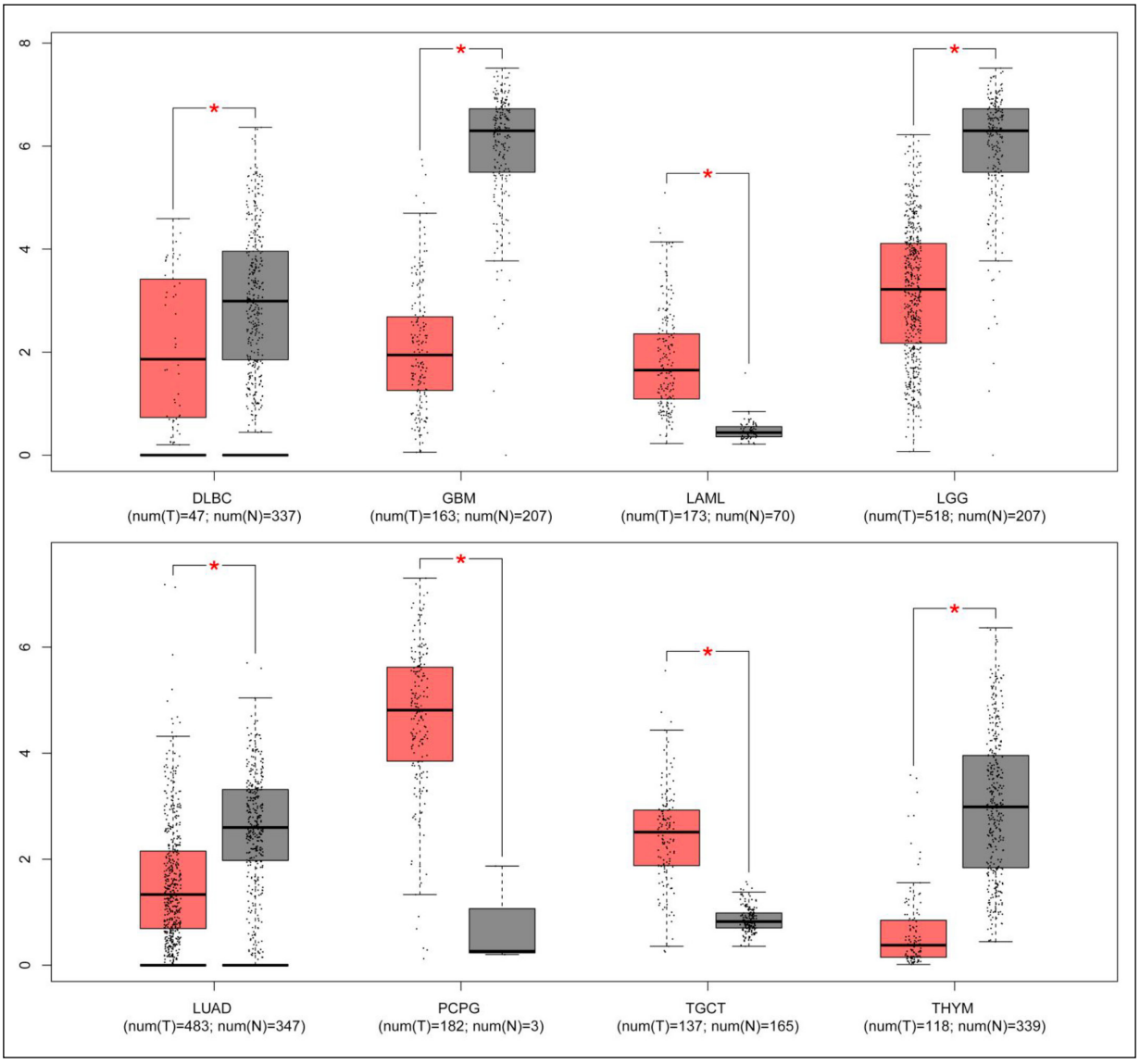

Figure 6. TCGA dataset analysis for the differential expression of MIAT between cancer tissue and normal tissue.

Wang et al[26] demonstrated that MIAT was involved in promoting the progression of acute myeloid leukaemia. Qu et al[30] suggested MIAT as an oncogenic lncRNA that promoted proliferation and metastasis of clear cell renal cell carcinoma. Additionally, Shao et al[32] reported that MIAT may act as a potential biomarker and novel therapeutic target for patients with ovarian cancer. However, because the sample sizes of the abovementioned studies were small, their conclusions should be interpreted cautiously due to limited study power.

Meta-analysis is a quantitative method combining related information from different studies to assess cancer-associated prognostic markers[42]. We conducted a meta-analysis with 14 studies, including 1573 enrolled cancer patients, to explore the prognostic value of lncRNA MIAT in multiple cancers. The results of the present study indicated that elevated lncRNA MIAT expression was significantly related to worse survival outcomes (OR=3.13, 95% CI: 2.47-3.96, $p<0.05$), regardless of the cancer type, sample size, and follow-up time. In addition, high lncRNA MIAT expression was positively associated with tumour size (OR=1.67, 95% CI: 1.24-2.26, $p<0.05$), advanced clinical stage (OR=4.79, 95% CI: 3.38-6.79, $p<0.05$), regardless of the cancer type, lymph nodes metastasis (OR=7.33, 95% CI: 4.61-11.67, $p<0.05$), and distant metastasis (OR=2.62, 95% CI: 1.88-3.66, $p<0.05$). Sensitivity analysis indicated that our results were stable, and

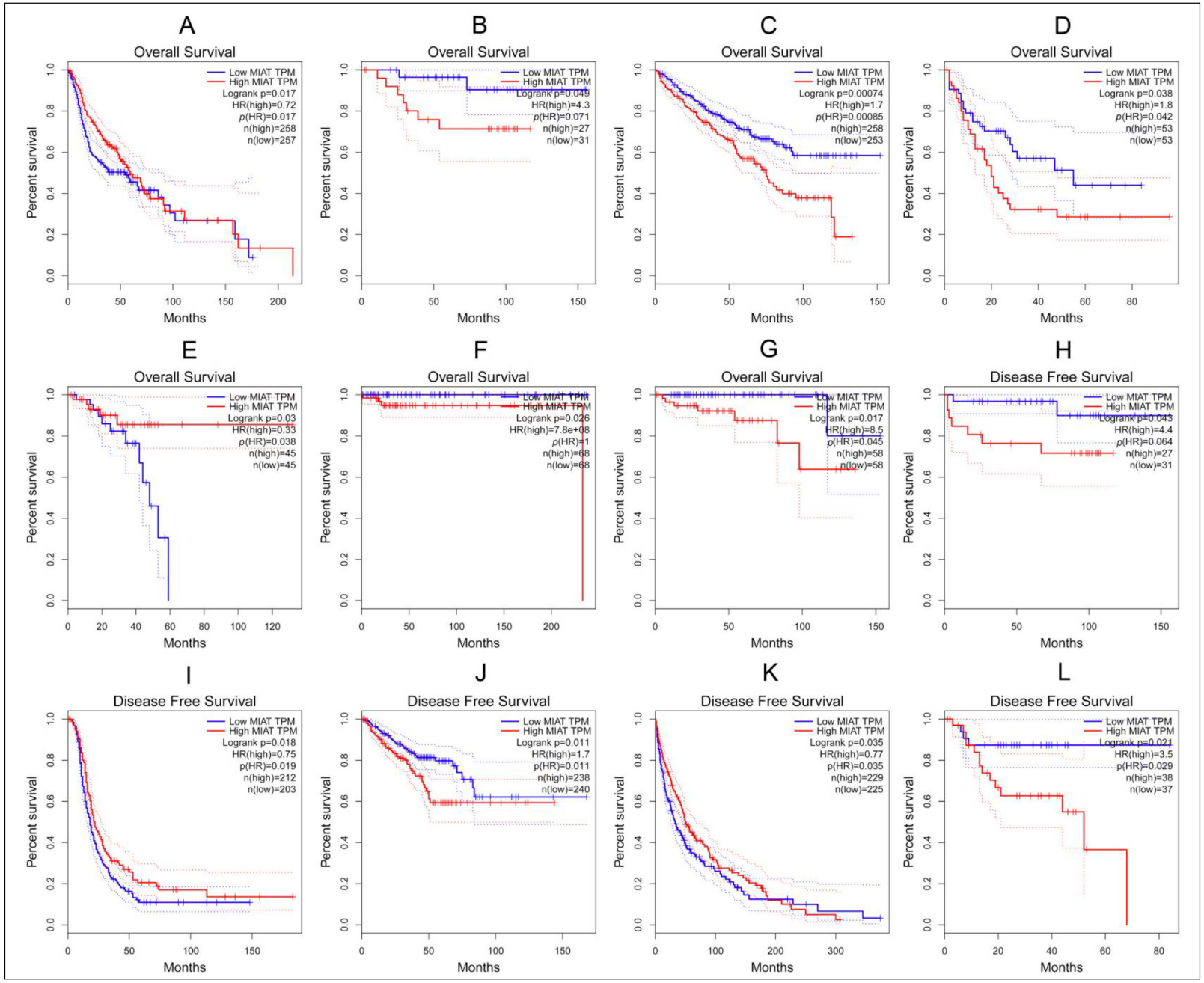

Figure 7. TCGA dataset analysis for the OS/DFS of MIAT in various cancers.

Table IV. LncMIAT/miRNA/target gene axis in tumorigenesis of cancers.

LncRNA	miRNAs	Target genes	Cancer type	Biological functions	PMID
LncMIAT	miR-495	-	Acute myeloid leukemia	Promotes the progression	31698307
LncMIAT	-	DLG3	Breast cancer	Promotes progression	32593652
LncMIAT	-	OCT4	Breast cancer	Decreases sensitivity to therapy	29914974
LncMIAT	miR-29c	COX2	Breast cancer	Promotes progression	29345338
LncMIAT	miR-155-5p	DUSP7	Breast cancer	Promotes progression	29100300
LncMIAT	-	PI3K/AKT	Cervical cancer	Promotes proliferation and migration	32239132
LncMIAT	miR-551b-3p	CCND1	Cholangiocarcinoma	Promotes the proliferation	32064660
LncMIAT	miR-29c	LOXL2	Clear Cell Renal Cell Carcinoma	Promotes proliferation and metastasis	30041179
LncMIAT	miR-132	Derlin-1	Colorectal cancer	Promotes growth and metastasis	29686537
LncMIAT	-	MMP-2/9	Esophageal cancer	Promotes cell invasion and migration	32266022
LncMIAT	miR-1301-3p	INCENP	Esophageal cancer	Promotes progression	31943174
LncMIAT	miR-141	DDX5	Gastric cancer	Promotes growth and metastasis	29540201
LncMIAT	miR-29a-3p	HDAC4	Gastric cancer	Promotes progression	29039602
LncMIAT	miR203a	HIF1α	Hepatocellular carcinoma	Potentiates the therapeutic effect	32468055
LncMIAT	miR-22-3p	SIRT1	Hepatocellular carcinoma	Promotes proliferation	31503007
LncMIAT	miR-520d-3p	EPHA2	Hepatocellular carcinoma	Promotes progression	30551417
LncMIAT	miR-214	-	Hepatocellular carcinoma	Promotes proliferation and invasion	29097358
LncMIAT	miR-150	-	Melanoma	Promotes the growth	32300960
LncMIAT	-	PI3K/AKT	Melanoma	Promotes migration and invasion	30614798
LncMIAT	miR-29b	-	Myeloma	Promotes growth	30967527
LncMIAT	miR-128-3p	PELI3	Non-small-cell lung cancer	Promotes progression	32556677
LncMIAT	miR-139-5p	MMP2	Non-small-cell lung cancer	Promotes migration and invasion	32345777
LncMIAT	miR-1246	-	Non-small-cell lung cancer	Promotes progression	31298331
LncMIAT	-	TDP43	Non-small-cell lung cancer	Promotes the growth and metastasis	31081093
LncMIAT	miR-149-5p	FOXM1	Non-small-cell lung cancer	Promotes progression	32742195
LncMIAT	miR-184	-	Non-small-cell lung cancer	Promotes proliferation	31897168
LncMIAT	miR-34a	PI3K/AKT	Non-small-cell lung cancer	Promotes cells to gefitinib	29487526
LncMIAT	-	MMP9	Non-small-cell lung cancer	Promotes proliferation and metastasis	29228680
LncMIAT	miR-133a-5p	MYO1B, SGK1 and WNT9A	Non-small-cell lung cancer	Promotes progression	29795987
LncMIAT	miR-150	ZEB1	Non-small-cell lung cancer	Promotes cell invasion	28843520
LncMIAT	miR-141-3p	SIX1	Osteosarcoma	Promotes progression	32196573
LncMIAT	miR-150-5p	ZEB1	Osteosarcoma	Promotes progression	30655889
LncMIAT	miR-128-3p	VEGFC	Osteosarcoma	Promotes progression	30629798
LncMIAT	miR-150-5p	-	Ovarian Cancer	Promotes growth and migration	32186927
LncMIAT	miR-330-5p	-	Ovarian cancer	Promotes cell proliferation	30393480
LncMIAT	miR-133	-	Pancreatic carcinoma	Promotes proliferation and metastasis	29772434
LncMIAT	miR-212	-	Papillary thyroid cancer	Promotes progression	31404776
LncMIAT	miR-324-3p	LASP1	Papillary thyroid cancer	Promotes progression	31372094

no publication bias was found using Egger's test. Moreover, the results from the TCGA dataset revealed that MIAT was differentially expressed in tumours than in normal tissue and that a higher MIAT expression predicted the worse OS and DFS. All these data indicated that lncRNA MIAT may serve as a diagnostic marker or therapy target in cancer management. Additionally, the molecular regulation of cancer development may help reveal underlying mechanisms of the actions of lncRNA MIAT in regulating the prognosis of various cancers (Table IV).

This meta-analysis had several limitations. First, only 14 reports were included in the meta-analysis, which could have decreased its credibility. Secondly, although we used Begg's funnel plots and Egger's test and no publication bias was observed, a potential publication bias may exist. Studies with positive data were more likely to be published. Last, although we strictly followed the **PRISMA guidelines** to conduct this meta-analysis, the current research was not registered, and minor deviations might have occurred. Therefore, further investigation is needed in these areas.

Conclusions

We found that higher lncRNA MIAT expression was markedly associated with less favourable clinical outcomes such as larger tumour sizes, advanced clinical stage, and metastasis. These observations imply that lncRNA MIAT may be a potential biomarker for cancer prognosis. More well-designed studies with high-quality data and larger sample sizes are needed to validate our results.

Ethics Approval

This meta-analysis was approved by the Second Xiangya Hospital of Central South University Committee for Clinical Research and all methods were carried out in accordance with the Declaration of Helsinki.

Informed Consent

Obtained.

Availability of Data and Materials

The datasets used and/or analyzed are available from the corresponding author upon reasonable request.

Conflict of Interest

The authors declare that they do not have any competing interests.

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Authors' Contributions

JZ and YZ conceived and designed the manuscript, and also critically revised it. YZ and BW conducted the experiments and drafted the manuscript. YZ, YD, YL, ZT, BJ and BW contributed to the revision of the manuscript. All of the authors have read and approved the final manuscript.

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