REVIEW

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Long Non-Coding RNA SNHG22 in Prognosis for Solid Tumors: A Systematic Review and Meta-Analysis

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Abstract

Objectives: Small nucleolar RNA host gene 22 (*SNHG22*) is a novel long non-coding RNA (lncRNA) that functions as an oncogene and promotes the progression of various cancers. This pooled analysis aimed to clarify the prognostic role of *SNHG22* in solid tumors and to explore its correlation with disease characteristics. **Methods:** We conducted a comprehensive search in databases such as PubMed/MEDLINE, Web of Science, Cochrane Library, and Google Scholar for relevant articles published until January 8, 2025. We combined individual data to estimate the overall hazard ratio (HR) for cancer prognosis. Additionally, We assessed the relationships between *SNHG22* expression levels and patient characteristics using the odds ratio (OR). **Results:** Nine studies involving 779 patients participated in the analysis. Patients with *SNHG22* overexpression exhibited poorer overall survival (HR=2.44, 95% confidence interval [CI]: 1.98-3.01, I^2=0%) and recurrence-free survival (HR=2.60, 95%CI: 1.69-4.00, I^2=0%) compared to those with lower levels. Furthermore, higher *SNHG22* expression was significantly associated with larger tumor size (OR=2.65, 95%CI: 1.13-6.22), lymph node metastasis (OR=2.12, 95%CI: 1.16-3.86), and advanced disease stages (OR=2.54, 95%CI: 1.73-3.72). **Conclusion:** The upregulation of *SNHG22* is associated with shorter survival outcomes, increased tumor size, lymph node metastases, and more advanced tumor stages.

Keywords: *SNHG22*- cancers- prognostics- meta-analysis

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Introduction

Cancer is a burden disease globally, whereas the number of cases is increasing yearly, most cases appear at advanced stages, and the five-year survival is still low [1,2]. Thus, seeking new biomarkers that serve as therapeutic targets and assist cancer diagnostics and prognostics is urgently needed. Long non-coding RNAs have been attracted and intensively studied recently. These are RNA molecules longer than 200 nucleotides involved in chromatin-based mechanisms and RNA cross-talk to regulate gene transcription and post-transcriptional processes [3]. Consequently, dysregulation of lncRNAs is associated with numerous human diseases, including cancers.

SNHG is a group of lncRNAs (SNHG1-33) that are mainly overexpressed in various tumors and regulate transcription factors, microRNA function, mRNA translation, ubiquitination, and DNA methylation, thereby playing critical roles in cell proliferation, angiogenesis, tumorigenesis, invasion, metastasis, and progression of cancers [4]. Among SNHG members, *SNHG22* was recently discovered and highlighted as a novel target. Fang and colleagues demonstrated that *SNHG22* is expressed at high levels in breast tumors and facilitates the malignant phenotypes by regulating the miR-324-3p/SUDS3 axis, opening its diagnostic potential [5]. Moreover, Li and colleagues proved that *SNHG22* can bind miR-429 and regulate the SESN3 axis to promote progression in esophageal squamous cell carcinoma [6]. Nevertheless, some opposite results exist (*SNHG22* down-regulated in osteosarcoma and inhibited cell proliferation, migration, and invasion in a mouse model) [7], emphasizing that further studies and explorations are needed. We systematically reviewed and aimed to assess the prognostic role of *SNHG22* in solid tumors and explore correlations of its expression levels with the disease features.

Materials and Methods

We conducted the meta-analysis according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [8].

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Literature search and selection

We performed a literature search on PubMed/MEDLINE, Web of Science, Cochrane Library, and Google Scholar for eligible articles up until January 8, 2025. The search terms used included "*SNHG22*", "small nucleolar RNA host gene 22", "SCARNA17", and "SCARNA17HG". Additionally, We reviewed the citations of potential studies to identify any additional articles. We utilized EndNote software to eliminate duplicates, resulting in 179 records (see Figure 1). Following this, We screened the titles and abstracts of the remaining articles, excluding 68 studies that included retracted papers, reviews, and those unrelated to cancer research. Of the 18 assessed in detail, We found one duplicated while eight lacked original data. Ultimately, We included nine studies in the meta-analysis that measured *SNHG22* expression in human cancer samples and provided prognostic data.

Quality assessment and data extraction

Three investigators independently evaluated the quality of the included studies using the Newcastle-Ottawa Scale (NOS), focusing on three aspects: selection (4 points), comparability (2 points), and outcome (3 points) [9]. A study could achieve a maximum of 2 points in the comparability if the treatment and demographic features (such as age and gender) between the two groups (low and high *SNHG22* levels) were similar. Studies with an NOS score of six points or higher were rated high quality.

Data extraction from the articles included details such as authors' names, year of publication, country, cancer type, clinical stage, treatment method, sample type, sample size, techniques used to detect *SNHG22*, control gene, cut-off values, HR values, and follow-up duration. If data was not directly extractable, We used Engauge Digitizer software version 12.1 to extrapolate data from survival curves and calculate HR values according to Tierney's recommendations [10]. Additionally, We extracted the number of true positives, false positives, true negatives, and false negatives for feature groups, including age, gender, clinical stage, tumor size, lymph node metastasis, and tumor differentiation, to calculate OR indices.

Statistical analysis

We employed a random-effects model to combine individual data and estimate the pooled HR value to aid prognosis assessment. An HR value greater than 1 indicates a poor prognosis associated with high *SNHG22* expression. An HR of less than 1 suggests a better prognosis. An HR of 1 signifies no significant difference in survival between the two groups. We assessed heterogeneity among studies using Higgins & Thompson's I^2-metric. In cases of substantial heterogeneity (I^2>50%), We applied the Leave-One-Out statistic to identify outliers and determine sources of influence. Moreover, We conducted a linear regression and utilized a funnel plot asymmetry test to evaluate the potential for publication bias. If bias was present, We employed the Trim-and-Fill statistic to impute missing studies and estimate the adjusted HR value. Furthermore, We summarized OR values to assess the associations between *SNHG22* levels and clinical characteristics. All statistical analyses were performed following the guidance of Shim and Harrer [11, 12], utilizing R version 4.4 software (R Foundation, Vienna, Austria) along with the 'meta' package. A p-value less than 0.05 indicates statistical significance.

Results

Characteristics of included studies

All nine studies employed polymerase chain reaction to measure *SNGH22* expression in tumor tissues derived

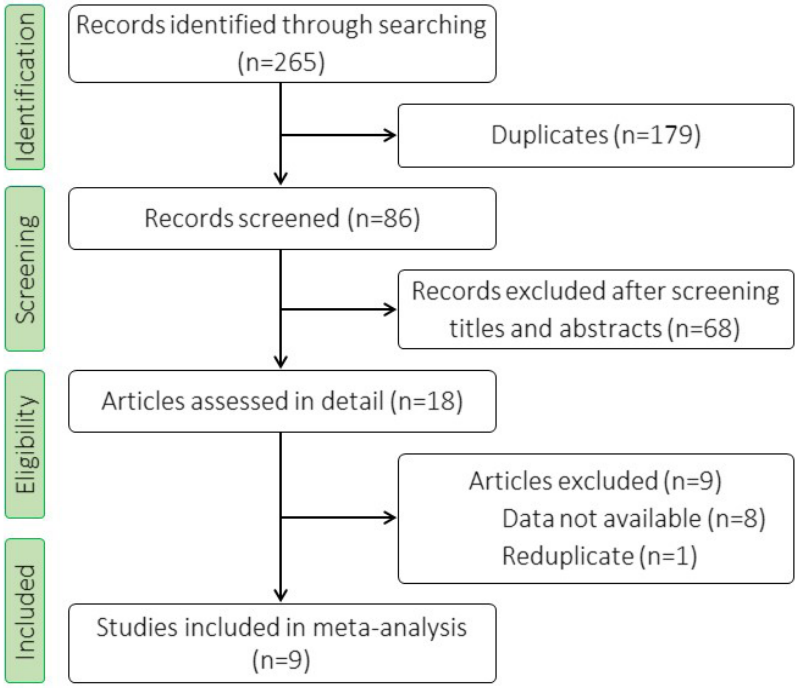

Figure 1. Database Searching and Study Selection

from surgery or serum samples and assessed its correlation with overall survival (OS) [13-21]. Two studies presented data on recurrence-free survival (RFS), and seven showed associations of *SNHG22* levels with clinical traits (Table 1). The total number of patients included in the meta-analysis was 779, including 377 low and 402 high-expression groups. A NOS score greater than or equal to six indicates that all studies are high quality.

Association of SNHG22 expression with survival outcomes

The analyzed results indicated that high expression of *SNHG22* is associated with shorter OS (HR=2.44, 95%CI: 1.98-3.01). Similarly, enhanced *SNHG22* level is a poor prognosis factor for RFS (HR=2.60, 95%CI: 1.69-4.00). No heterogeneity was found in analyses (I^2=0%, Figure 2A). Furthermore, in subgroups categorized by cancer, sample size, follow-up duration, data extraction method, and control gene, there was no significant heterogeneity and differences in HR estimates among the groups (Table 2). For the potential publication bias (Figure 2B), We used the Trim-and-Fill statistics to impute missing studies. Subsequently, We noted an adjusted HR value of 2.25 (95%CI: 1.91-2.65) for both survival outcomes (Figure 2C).

Association of SNHG22 expression with clinical characteristics

Among six analyses (Figure 3), We recorded that *SNHG22* expression did not correlate with patients' age, gender, and tumor differentiation. Notably, aberrant *SNHG22* was observed more frequently in the larger tumor size (above 5cm, Figure 3D) with statistical significance (OR=2.65, 95%CI: 1.13-6.22). Moreover, We found that high *SNHG22* levels are associated with lymph node

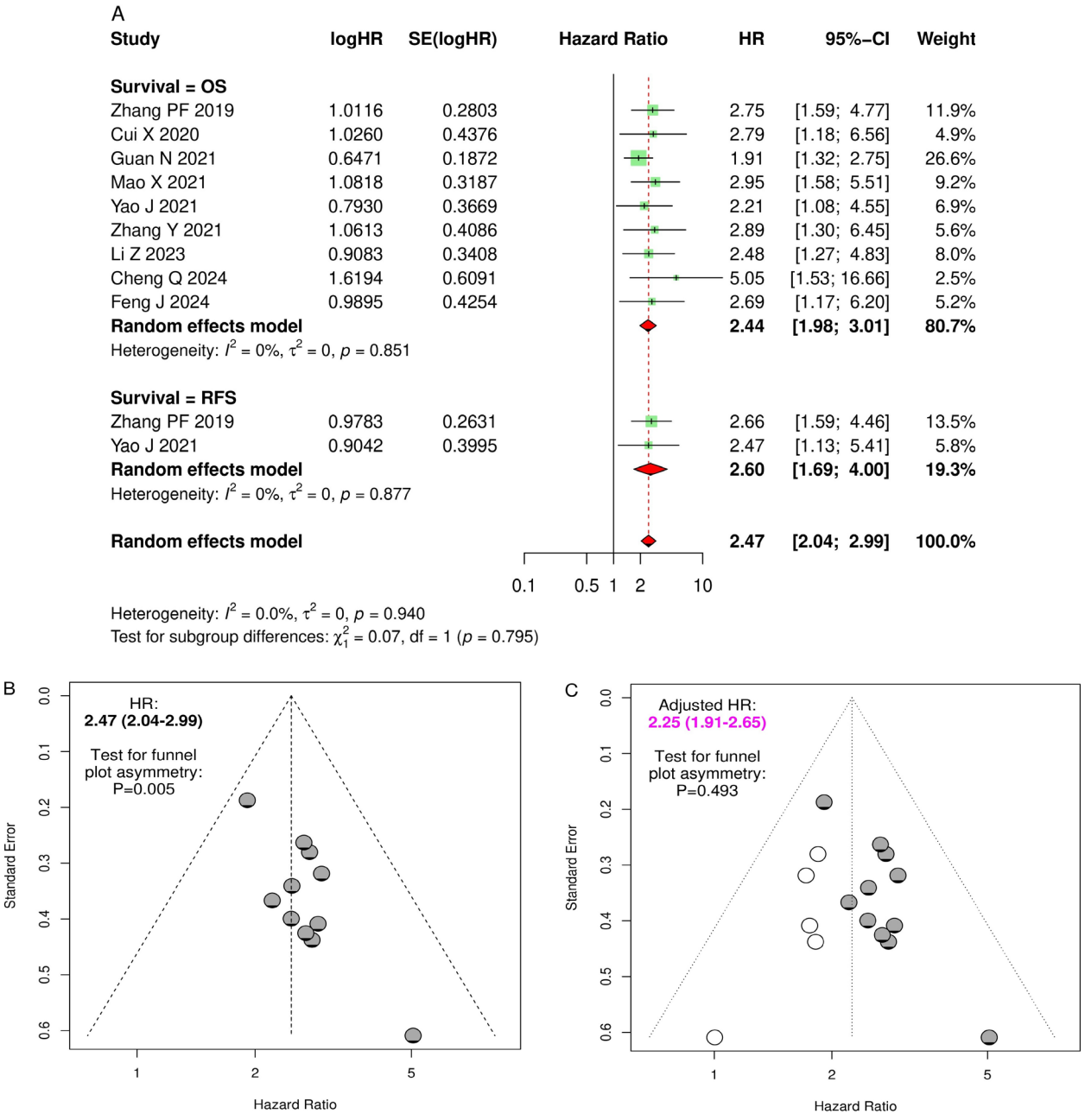

Figure 2. Forest Plots of HR for Survival Outcomes (A) and funnel plot asymmetry tests before (B) and after adjusting for publication bias (C)

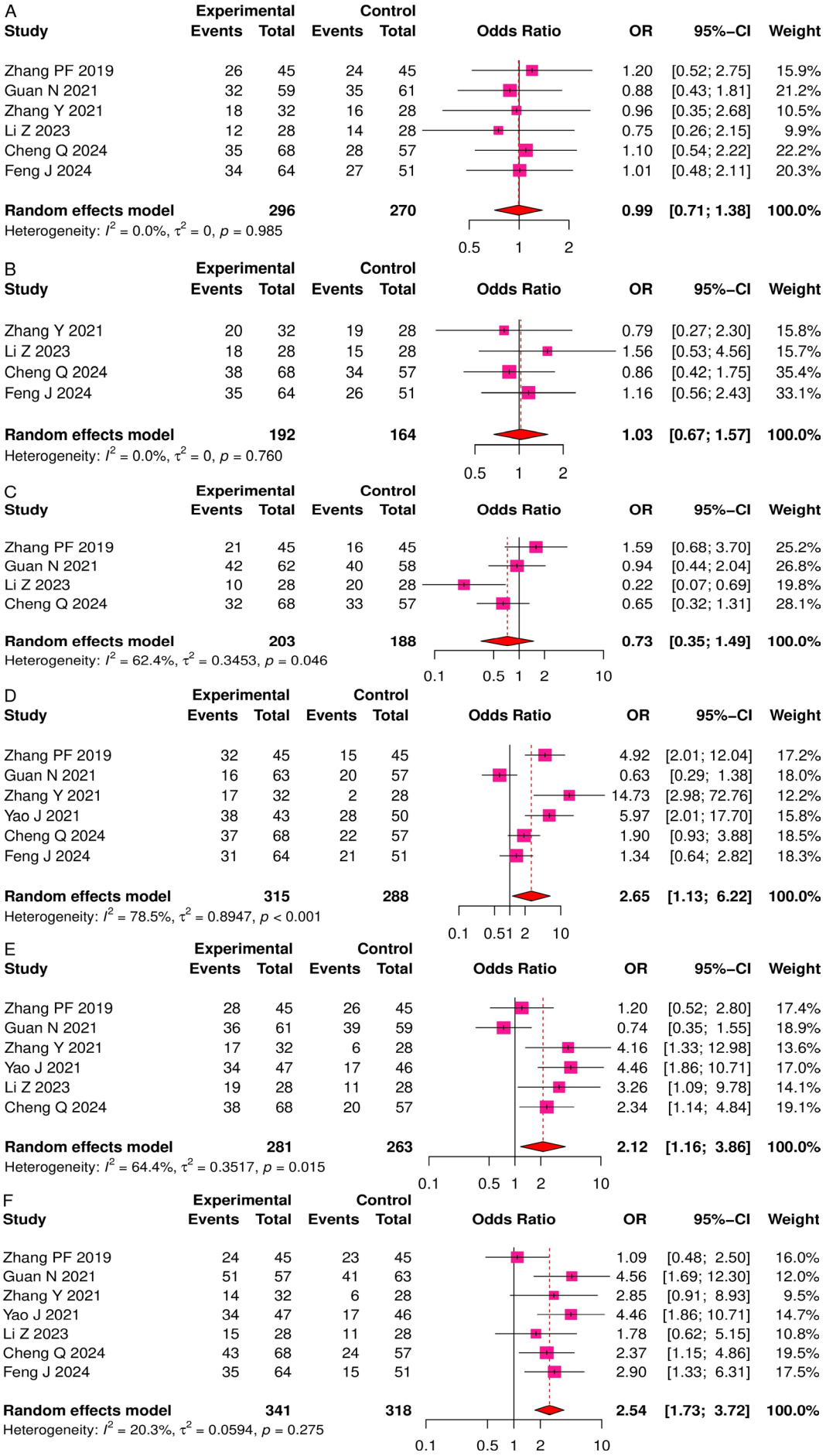

Figure 3. Association of *SNHG22* Expression with Patients' age (A), gender (B), tumor differentiation (C), tumor size (D), lymph-node metastasis (E), and clinical stages (F)

metastasis (OR=2.12, 95%CI: 1.16-3.86, Figure 3E) and advanced clinical stages (OR=2.54, 95%CI: 1.73-3.72, Figure 3F).

Discussion

Previous studies have demonstrated that *SNHG22* is expressed aberrantly in tumor tissues and functions as an oncogene. It regulates numerous microRNAs (such as miR-27b-3p, miR-324-3p, miR-429, miR-361-3p, miR-101-3p, miR-200c-3p, miR-128-3p, miR-2467, and miR-16-5p), genes, and signaling pathways (including SUDS3, SESN3, E2F2, E2F3, Gal-1, HMGA1/Wnt/β-Catenin, and Notch1), thereby promoting cancer growth, progression, and resistance to therapy [5, 6, 13-21]. Conversely, silencing *SNHG22* inhibits cell proliferation in vivo and increases the sensitivity of cancer cells to chemotherapy and apoptosis [13, 17-19, 21]. Therefore, *SNHG22* may serve as a clinical biomarker and therapeutic target. However, comprehensive evaluations of *SNHG22* are currently lacking. We performed a systematic review and meta-analysis of nine studies, finding that high levels of *SNHG22* are associated with advanced stages of cancer, lymph node metastasis, and large tumor size. Notably, consistent evidence across these studies indicates that overexpression of *SNHG22* is an unfavorable prognostic factor for OS and RFS outcomes. Despite some publication bias, the adjusted HR value remains significant (Figure 2C). Besides, these results are supported by two studies reviewed but not eligible for analysis [5, 6]. Thus, these findings will help guide future studies and trials before establishing *SNHG22* as a reliable clinical biomarker.

To our knowledge, this is the first review clarifying the prognostic role of *SNHG22* in solid tumors, though some limitations exist. Firstly, all studies included in the analyses were from China. So, the conclusions drawn from this analysis are just reasonable for patients in China and East Asia. Secondly, the number of cancer types included in the meta-analysis is limited (gastric, ovarian, colorectal cancer, hepatocellular carcinoma, non-small cell lung cancer, and glioma). Thirdly, some individual studies did not provide HR values directly (Table 1). We just obtained these values by using the Engauge Digitizer software to extrapolate from survival curves that might affect overall HR estimates. Hence, We suggest performing global experimental studies that cover extensive types of cancers to provide more evidence-based information and confirm our findings. Furthermore, assessments on other specific regimens like chemotherapy, radiotherapy, and targeted therapies are encouraged. Finally, standardization of the RT-qPCR method, which includes sample extraction, specific primer pair, probe, normalization gene, and a specific cut-off, will increase reproducibility and help in more accurate assessments.

In conclusion, this meta-analysis suggests that overexpression of *SNHG22* correlates with large tumor size, lymph node metastasis, and advanced cancer stages. Besides, high *SNHG22* levels predict poor survival outcomes in solid tumors that can serve as a prognostic marker clinically.

Table 1. Characteristics of Included Studies

Author	Year	Country	Cancer type	Clinical stage	Treatment	Sample type	Sample size	Method	Control gene	Cut-off	Maximum follow-up	HR (95%CI)	Survival	Data extraction	CCA	NOS score	Ref
Zhang PF	2019	China	OC	I-IV	Surgery	Tissue	90	RT-qPCR	GAPDH	Median (5.63)	60 Months	2.75 (1.59-4.77)	OS	Indirect	Yes	8	13
												2.66 (1.59-4.46)	RFS				
Cui X	2020	China	GC	I-IV	Surgery	Tissue	60	RT-qPCR	GAPDH	Mean (3.13)	60 Months	2.79 (1.18-6.56)	OS	Indirect	No	7	14
Guan N	2021	China	OC	I-IV	Surgery	Tissue	120	RT-qPCR	GAPDH, U6	Median (3.38)	100 Months	1.91 (1.32-2.75)	OS	Direct	Yes	7	15
Mao X	2021	China	GC	NA	Surgery	Tissue	60	RT-qPCR	U6, β actin	Median	89 Months	2.95 (1.58-5.51)	OS	Indirect	No	7	16
Yao J	2021	China	CRC	I-IV	Surgery	Tissue	93	RT-qPCR	U6, β actin	Median (6.10)	110 Months	2.21 (1.08-4.55)	OS	Direct	Yes	7	17
												2.47 (1.13-5.41)	RFS				
Zhang Y	2021	China	HCC	I-IV	Surgery	Tissue	60	RT-qPCR	GAPDH	NA	156 Months	2.89 (1.30-6.45)	OS	Indirect	Yes	7	18
Li Z	2023	China	GC	I-IV	Surgery	Tissue	56	RT-qPCR	GAPDH, U6	Median (3.48)	115 Months	2.48 (1.27-4.83)	OS	Indirect	Yes	8	19
Cheng Q	2024	China	NSCLC	I-IV	NA	Serum	125	RT-qPCR	GAPDH	NA	60 Months	5.05 (1.53-16.66)	OS	Direct	Yes	6	20
Feng J	2024	China	Glioma	I-IV	Surgery	Tissue	115	RT-qPCR	GAPDH, U6	Mean (2.19)	60 Months	2.69 (1.17-6.20)	OS	Direct	Yes	7	21

Abbreviation: 95%CI, 95% Confidence interval; CCA, Clinicopathological characteristics analysis; CRC, Colorectal cancer; GAPDH, Glyceraldehyde-3-phosphate dehydrogenase; GC, Gastric cancer; HCC, Hepatocellular carcinoma; HR, Hazard ratio; NA, Not available; NOS, Newcastle-ottawa scale; NSCLC, Non-small cell lung cancer; OC, Ovarian cancer; OS, Overall survival; Ref., Reference; RFS, Recurrence-free survival; RT-qPCR, Reverse transcriptase quantitative polymerase chain reaction.

Table 2. Subgroup Meta-Analyses for Overall Survival

Variable		No. of study	No. of patient	HR (95%CI)	I^2, %	p-value*	p-value**
Cancer group							
	Gastrointestinal	5	329	2.64 (1.92-3.65)	0	0.978	0.640
	Other	4	450	2.37 (1.72-3.27)	6.1	0.363	
Sample size							
	≤100	6	419	2.67 (2.02-3.53)	0	0.993	0.621
	>100	3	360	2.34 (1.49-3.67)	24.3	0.267	
Follow-up							
	≤60 months	4	390	2.92 (1.99-4.29)	0	0.825	0.270
	>60 months	5	389	2.26 (1.75-2.90)	0	0.746	
Data extraction method							
	Direct	4	453	2.17 (1.61-2.91)	0	0.450	0.261
	Indirect	5	326	2.76 (2.04-3.73)	0	0.997	
Control gene							
	GAPDH	4	335	2.97 (2.03-4.34)	0	0.835	0.364
	GAPDH/U6	3	291	2.10 (1.56-2.84)	0	0.659	
	U6/β-actin	2	153	2.61 (1.63-4.18)	0	0.552	

Note: *for heterogeneity; **significance of HR values between groups. Abbreviation: 95%CI, 95% Confidence interval; GAPDH, Glyceraldehyde-3-phosphate dehydrogenase; HR, Hazard ratio.

Author Contribution Statement

Thang Thanh Phan: conceptualization, investigation, data curation, formal analysis, methodology, writing-original draft, and writing-review and editing. Hang Thuy Nguyen: investigation, formal analysis, and writing-original draft. Phu Thien Truong: investigation, formal analysis, and writing-original draft. Anh Tu Le: investigation, formal analysis, and writing-original draft. Loc Duc Nguyen: formal analysis, writing-original draft, and writing-review and editing. Son Truong Nguyen: conceptualization, methodology, supervision, and writing-review and editing. Bao Thy Vuong: conceptualization, methodology, supervision, and writing-review and editing.

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Not applicable.

Approval

The study does not require ethics committee approval or consent forms. Furthermore, it is not part of an approved student thesis.

Availability of data

All data generated or analyzed during this study are included in this published article.

Registration

The study is not registered in any registration database.

Conflicts of Interests

The authors declared that no conflicts of interest exist.

Abbreviations

95%CI: 95% Confidence interval; CCA, Clinicopathological characteristics analysis; CRC, Colorectal cancer; GAPDH, Glyceraldehyde-3-phosphate dehydrogenase; GC, Gastric cancer; HCC, Hepatocellular carcinoma; HR, Hazard ratio; NA, Not available; NOS, Newcastle-ottawa scale; NSCLC, Non-small cell lung cancer; OC, Ovarian cancer; OS, Overall survival; Ref., Reference; RFS, Recurrence-free survival; RT-qPCR, Reverse transcriptase quantitative polymerase chain reaction.

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