EJMO

DOI: 10.14744/ejmo.2023.24253
EJMO 2023;7(4):298–305

Systematic Meta Analysis

The Prognostic Significance of miR-613 in Malignant Tumors and Association with Clinical Characteristics: A Systematic Review and Meta-Analysis

Vinh Thanh Tran,[1#] Thang Thanh Phan, [1#] Khanh Quang Huynh,[2] Toan Trong Ho,[1] Suong Phuoc Pho,[1] Hang Thuy Nguyen,[3] Hung Duy Tran,[1] Lan Thi Nguyen,[1] Thang Hong Pham,[1] Binh Thanh Le,[4] Thuc Tri Nguyen,[4] Son Truong Nguyen[4]

[1]The Laboratory D Unit, Cancer Center, Cho Ray Hospital, HCMC, Vietnam
[2]The Breast Unit, Cancer Center, Cho Ray Hospital, HCMC, Vietnam
[3]Department of Clinical Pathology, Cho Ray Hospital, HCMC, Vietnam
[4]Department of General Director, Cho Ray Hospital, HCMC, Vietnam

#The authors contributed equally to the study.

Abstract

Objectives: Previous studies have shown that microRNA-613 (miR-613) functions as a tumor suppressor gene in various organ tissues. Our meta-analysis aimed to systematically evaluate the prognostic role of miR-613 and its association with clinical characteristics of malignant tumors.

Methods: We searched the PubMed/MEDLINE, Web of Science, Cochrane Library, and Google Scholar databases for relevant studies until July 25, 2023. Then, We pooled individual data and estimated the overall Hazard ratio (HR) and Odds ratio (OR) of miR-613 for prognosis and patient characteristic linking evaluations, respectively.

Results: After selection, 14 eligible studies with 1510 patients enrolled in final analyses. The lower level of miR-613 expression is associated with advanced stages (OR=3.08, 95% confidence interval [CI]: 2.27-4.18), larger tumor size (OR=2.05, 95%CI: 1.11-3.78), and lymph-node metastasis (OR=3.62, 95%CI: 2.55-5.14). Notably, downregulated miR-613 is associated with inferior progression-free survival (adjusted HR=1.65, 95%CI: 1.31-2.10) and overall survival (adjusted HR=1.83, 95%CI: 1.59-2.11). No significant heterogeneity was found in the analyses (I2=0%, P-values were 0.473 and 0.685, respectively).

Conclusion: The results of this study indicate that low miR-613 expression is associated with advanced stages, larger tumor size, and lymph node metastasis in malignant tumors. Besides, low miR-613 is a poor prognosis indicator for PFS and OS.

Keywords: Cancers, miR-613, meta-analysis, prognostics

Cite This Article: *Tran VT, Phan TT, Huynh KQ, Ho TT, Pho SP, Nguyen HT, et al. The Prognostic Significance of miR-613 in Malignant Tumors and Association with Clinical Characteristics: A Systematic Review and Meta-Analysis. EJMO 2023;7(4):298–305.*

Recent advances in diagnosis and treatment, especially the appearance of targeted therapies, have improved the 5-year survival of cancers.[1] Despite that, survival rates of common cancers such as liver, lung, stomach, esophagus, pancreas, and brain are still low (5-40%).[1] Consequently, studying and seeking new biomarkers (tumor DNA and cells, DNA methylation, long non-coding RNAs, microRNAs...) that serve as novel therapeutic targets and assist current tests in the early diagnosis and prognosis of cancers is necessary. Among the molecular biomarkers, microRNAs (miR-21, miR-155, miR-222, Etc.) are highly attracted and studied as promising candidates.[2] After production, the mature microRNA binds to targeted mRNA genes, then inhibits the translation and initiation of gene cleavage.[2] In

Address for correspondence: Thang Thanh Phan, MD. The Laboratory D Unit, Cancer Center, Cho Ray Hospital, 201B Nguyen Chi Thanh Street, Dist. 5, Ho Chi Minh City, 700000, Vietnam
Phone: +84 283 855 4137 **E-mail:** thanhthangphan@gmail.com

Submitted Date: July 25, 2023 **Accepted Date:** November 19, 2023 **Available Online Date:** December 29, 2023

malignant cells, this physiological process is dysregulated by increasing oncogenic microRNA activity while restricting tumor suppressor microRNA, leading to tumorigenesis, invasion, migration, and metastasis.[2] One of the interested microRNAs, miR-613, has been shown to target multiple genes and pathways (cMET, CXCR4, KRAS, SPHK1/2, MMP9, CDK4/9/14, PDK1, E2F5, SOX9, ID4/PI3K/AKT, AXL/AKT, Jagged-1/Notch/CXCR4, DNMT3B/TIMP3/STAT1/FOXO1), and function as a tumor suppressor but downregulated in various cancers.[3-7] Thus, its expression suggests that miR-613 might be the clinically reliable biomarker. This meta-analysis aimed to evaluate the prognostic role of miR-613 and its association with cancer characteristics.

Methods

This meta-analysis was conducted following the guideline of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[8]

Database Searching and Study Selection

We searched the databases of PubMed/MEDLINE, Web of Science, Cochrane Library, and Google Scholar for eligible studies from inception to 25 July 2023. The keywords used in searching include "miR-613", "miR613", "miRNA-613", "miRNA613", "microRNA-613", and "microRNA613". In addition, We reviewed citation reports of potential studies to find more articles. After searching, relevant studies (n=3257) were managed by the EndNote software and filtered, removed duplicates (997 records, Fig. 1). By screening titles and abstracts, We excluded 2178, including retracted articles. Of the detailed assessment, 66 without required data, one with public data, and one with previously treated patients did not progress further. Ultimately, 14 studies with miR-613 expression and prognostic data enrolled in the meta-analysis.

Quality Assessment and Data Extraction

The quality of included studies was assessed by two investigators using the Newcastle-Ottawa Scale (NOS), which comprises selection (4 points), comparability (2 points), and outcome categories (3 points).[9] A study was awarded 2 points in the comparability aspect if similar in (1) demographic feature (age, gender) and (2) treatment method between the study (low miR-613) and control (high miR-613) arms. A greater than or equal to six points was classified as high quality. In case of no consensus on assessments, evaluators discussed with each other and determined the final decision.

Data extracted from articles include author names, year of publication, country, cancer type, disease stage, treatment method, sample type, sample size, techniques used in miR-613 detecting, reference gene, cut-off, HR values,

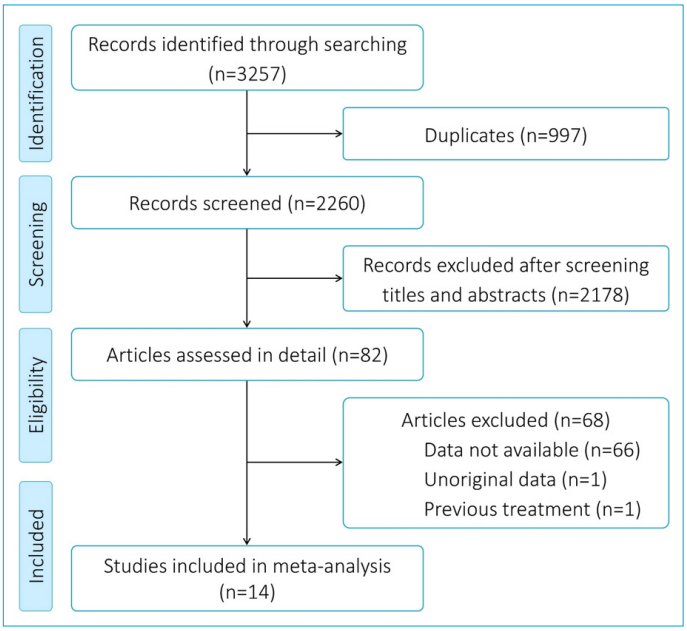

Figure 1. Database searching and study selection.

HR extraction method, and analysis model (multivariable or univariable that HR values have been adjusted for clinical confounders or not). Besides, We extracted the true-positive, false-positive, true-negative, and false-negative numbers corresponding to the clinical characteristics (age, gender, clinical stage, tumor size, lymph node metastasis, and tumor differentiation) to support association analyses. In case of not directly extractable, We used the Engauge Digitizer 12.1 software to extrapolate data from the Kaplan-Meier curves, then calculated HR values according to suggestions of Tierney.[10]

Statistical Analysis

All statistical analyses were performed with the guidance of Harrer and Shim,[11,12] using R v.4.3 software (R foundation, 1020 Vienna, Austria) and package meta. We used the random-effects model to estimate the overall HR value to support prognosis assessments. HR>1 indicates a poor prognosis of low miR-613 expression and vice versa for elevated gene expression. HR=1 is an indicator of no significant difference in survival time between groups. The heterogeneity of estimates between studies was measured by Higgins & Thompson's I2-statistic, which is substantial if I2>50%. We adopted the funnel plot asymmetry based on the linear regression test to detect potential publication bias. Once bias exists, We used the Trim-and-Fill statistics to impute missing studies, then calculated the adjusted HR values. For the association analyses between miR-613 expression and clinical features, We summarized OR values to give evaluations. The statistical analyses were significant if $p<0.05$.

Table 1. Characteristics of included studies

Author	Year	Country	Cancer type	Clinical stage	Treatment	Sample type	Sample size	Method	Ref. Gene	Cut-off	HR (95%CI)	Survival	HR extraction	Analysis model	CCA	NOS score	Ref.
Guan S	2016	China	ESCC	I-III	Surg	Tissue	109	RT-qPCR	U6	Mean (0.0016)	1.524 (1.095-2.123)	PFS	Direct	Multi	Yes	9	[13]
											1.692 (1.004-2.851)	OS					
Hu J	2016	China	CRC	A-D	Surg	Tissue	100	RT-qPCR	GAPDH	Mean (0.1805)	2.486 (1.169-5.286)	DFS	Indirect	Uni	Yes	9	[14]
											3.256 (1.403-7.556)	OS					
Li D	2016	China	NSCLC	I-IV	Surg	Tissue	56	RT-qPCR	U6	Mean (1.348)	3.829 (1.464-10.015)	OS	Indirect	Uni	No	8	[15]
Zhang X	2016	China	OC	I-IV	Surg	Tissue	236	RT-qPCR	U6	Median (3.25)	2.417 (1.771-10.871)	PFS	Direct	Multi	Yes	9	[16]
											2.215 (1.671-8.882)	OS					
Cai H	2017	China	PC	I-IV	Surg	Tissue	59	RT-qPCR	U6	Median (13.92)	2.398 (1.181-4.868)	OS	Indirect	Uni	Yes	9	[17]
Wang Y	2017	China	GBM	I-IV	Surg	Tissue	64	RT-qPCR	U6	Median	2.216 (1.194-4.112)	DFS	Indirect	Uni	Yes	9	[18]
											2.834 (1.273-6.309)	OS					
Zhang Y	2017	China	RB	I-IV	Surg, Chem, Rad	Tissue	45	RT-qPCR	U6	Median (0.592)	3.262 (1.168-9.109)	OS	Indirect	Uni	Yes	9	[19]
Jiang X	2018	China	HCC	I-IV	Surg	Tissue	64	RT-qPCR	GAPDH, U6	Median (0.549)	1.945 (1.195-3.165)	OS	Indirect	Uni	Yes	9	[20]
Sang Q	2018	China	Glioma	I-IV	Surg	Tissue	30	RT-qPCR	U6	Median (0.25)	3.488 (1.419-8.574)	OS	Indirect	Uni	No	8	[21]
Yang G	2018	China	RB	I-IV	Surg, Chem, Rad	Tissue	276	RT-qPCR	U6	Mean	2.69 (1.44-5.04)	OS	Direct	Multi	Yes	9	[22]
Zhu Y	2018	China	Osteosarcoma	I-IV	Surg	Tissue	211	RT-qPCR	U6	Median (0.364)	1.669 (1.275-2.184)	OS	Indirect	Uni	No	8	[23]
Liu H	2019	China	GC	I-IV	Surg	Tissue	176	RT-qPCR	U6	Mean	1.869 (1.195-2.924)	OS	Direct	Multi	Yes	9	[24]
Zhou N	2019	China	HCC	I-IV	Surg	Tissue	52	RT-qPCR	U6	Median (0.052)	2.378 (1.107-5.15)	OS	Direct	Uni	Yes	9	[25]
Luo J	2021	China	NSCLC	I-III	Surg	Tissue	32	RT-qPCR	U6	Median (0.675)	3.383 (0.672-10.033)	OS	Direct	Uni	Yes	9	[26]

Abbreviation: 95%CI: 95% Confidence interval; CCA, Clinical characteristic analysis; Chem, Chemotherapy; CRC, Colorectal cancer; DFS, Disease-free survival; ESCC, Esophageal squamous cell carcinoma; GAPDH, Glyceraldehyde-3-phosphate dehydrogenase; GBM, Glioblastoma; GC, Gastric cancer; HCC, Hepatocellular carcinoma; HR, Hazard ratio; Multi, Multivariate analysis; NOS, Newcastle-ottawa scale; NSCLC, Non-small cell lung cancer; OC, Ovarian cancer; OS, Overall survival; PC, Pancreatic cancer; PFS, Progression-free survival; Rad, Radiotherapy; RB, Retinoblastoma; Ref., Reference; RT-qPCR, Reverse transcriptase quantitative polymerase chain reaction; Surg, Surgery; Uni, Univariate analysis.

Results

Characteristics of Included Studies

Among 14 studies,[13-26] three studies demonstrated the role of miR-613 in predicting progression-free survival (PFS) and overall survival (OS),[13,16,18] one presented data of disease-free survival and OS,[14] while ten others exhibited data of OS[15,17,19-26] (Table 1). All studies detected miR-613 in tissue samples derived from surgery, using the polymerase chain reaction method, and obtained a NOS score above six. Eleven out of 14 studies showed correlations of miR-613 levels with clinical traits (details in Table S1). The total numbers included in the meta-analysis were 1510 patients.

The Prognostic Significance of miR-613

The pooled results indicated that the low miR-613 level is associated with shorter PFS/DFS (HR=1.86, 95%CI: 1.37-2.52, Fig. 2A) and OS time (HR=2.13, 95%CI: 1.79-2.53, Fig. 2B). Also, We found that overall estimates are highly consistent between studies (I2=0%, p were 0.473 and 0.685 for PFS and OS, respectively). By the data extraction and analysis methods, the heterogeneity within groups and the HR differences between groups are not statistically significant (Fig. 2C and 2D). However, a publication bias might be present in analyses (Fig. 3A and 3B). We used the Trim-and-Fill statistics to impute assumed studies (Fig. 3C and 3D) and noted an adjusted HR value of 1.65 (95%CI: 1.31-2.10, p<0.001) for PFS/DFS and 1.83 (95%CI: 1.59-2.11, p<0.001) for OS.

Association of miR-613 with Clinical Characteristics

As shown in Figure 4, the miR-613 expression did not correlate with patient age and gender. Significantly, low miR-613 levels are linked to the advanced disease stages (OR=3.08, 95%CI: 2.27-4.118, Fig. 4C), lymph-node metastasis (OR=3.62, 95%CI: 2.55-5.14, Figure 4D), and larger tumor size (OR=2.05, 95%CI: 1.11-3.78, Fig. 4E). Downregulation of miR-613 was observed more frequently in poorly differentiated tumors but not with significance (Fig. 4F).

Discussion

Increasing evidence expressed that miR-613 regulates multiple genes and functions as a tumor suppressor to inhibit cell proliferation, carcinogenesis, migration, invasion, and metastasis.[3] Nevertheless, miR-613 was targeted directly by the long noncoding or circular RNAs as HOTAIR, RMRP, MALAT1, UCA1, LINC00152, LINC00460, CircRIMS..., thus downregulated in numerous malignant tumors like hepatocellular carcinoma, gastric, lung, breast, thyroid, bladder, cervical cancers, glioma, retinoblastoma, and osteosarcoma.[3,4,27-30] Accordingly, the miR-613 expression might contrib-

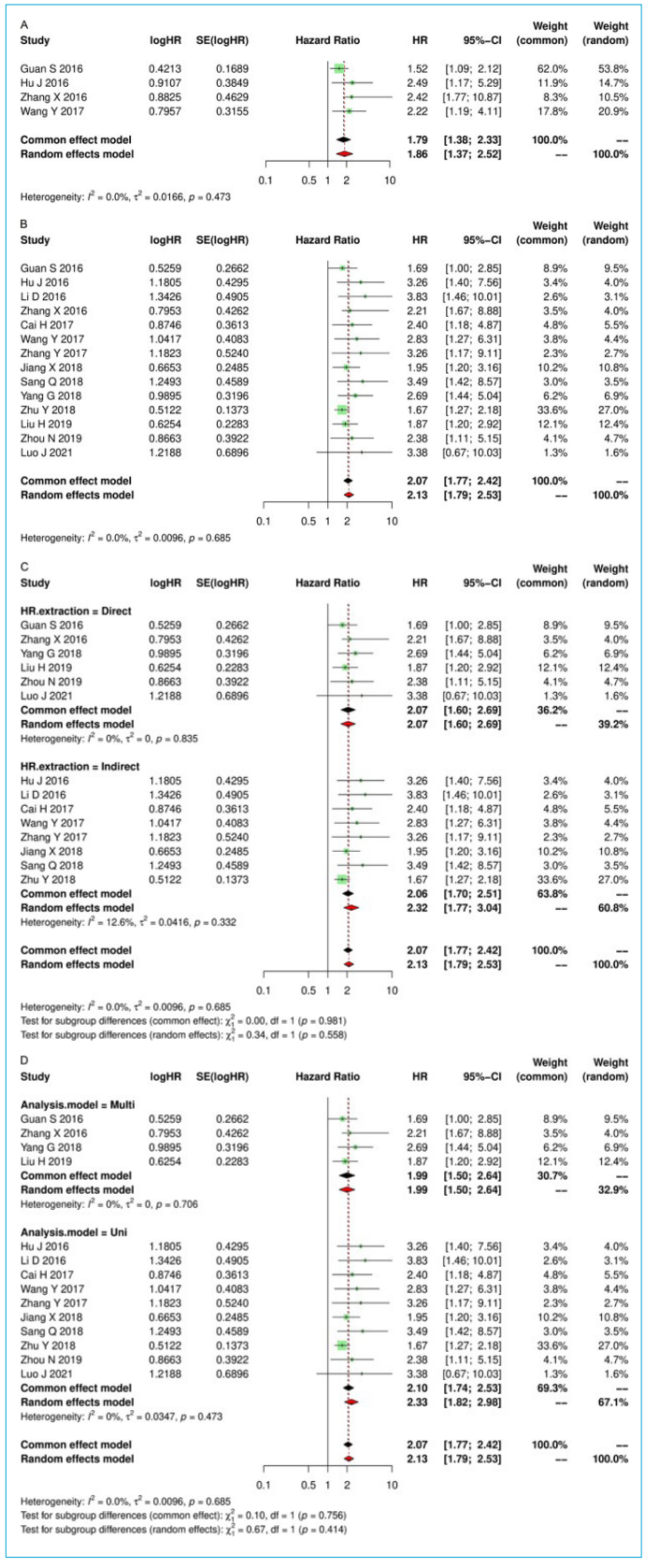

Figure 2. Forest plots of HR for progression-free survival **(a)** and overall survival **(b)**, overall survival by the data extraction **(c)** and analysis methods **(d)**.

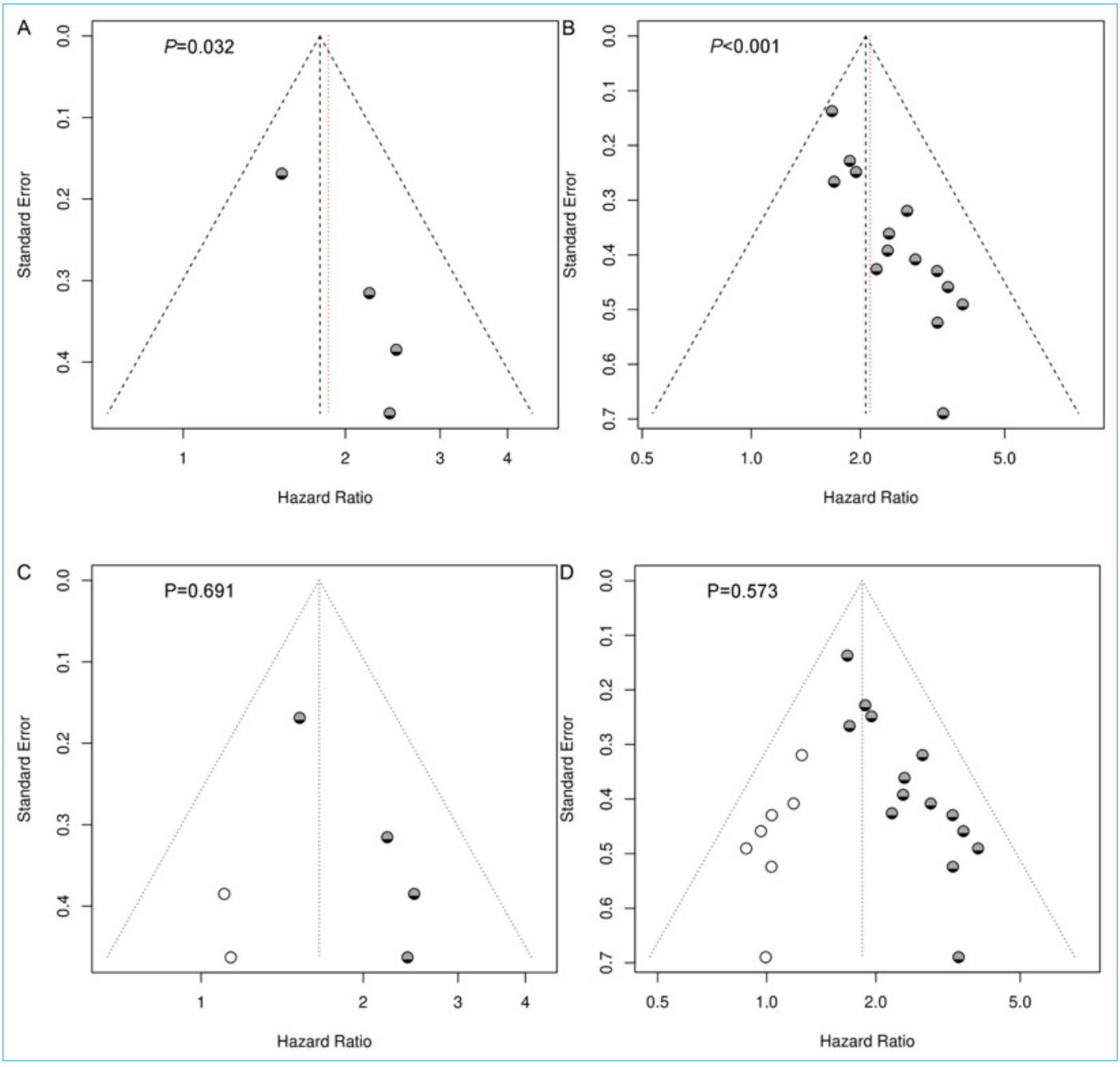

Figure 3. Funnel plot asymmetry tests for PFS and OS before **(a, b)** and after adjusting for publication bias **(c, d)**.

ute as a promising biomarker for diagnosis and prognosis, but no comprehensive evaluations have been made to date.

We conducted a systematic review and meta-analysis on 14 studies and noted that lower tissue miR-613 expression levels are related to advanced diseases, larger tumor size, and lymph node metastasis in cancers (Fig. 4). Impressively, We found highly consistent evidence across studies that low miR-613 is an unfavorable prognostic marker for PFS and OS regardless of data extraction methods (Fig. 2). Despite of publication bias existence, the adjusted HR values remain significant. Meanwhile, some reviewed studies but not eligible for this meta-analysis, where their results strengthen the hypothesis that low miR-613 is related to therapy resistance and poor prognosis.[5,31,32] Hence, these findings will lead the way for future studies before miR-613 becomes a prognostic biomarker clinically.

Regarding the limitations of meta-analysis, We suggest that subsequent studies should deal with liquid biopsy samples such as plasma, serum, body fluids, and urine, leading to practical and easy miR-613 testing in the real

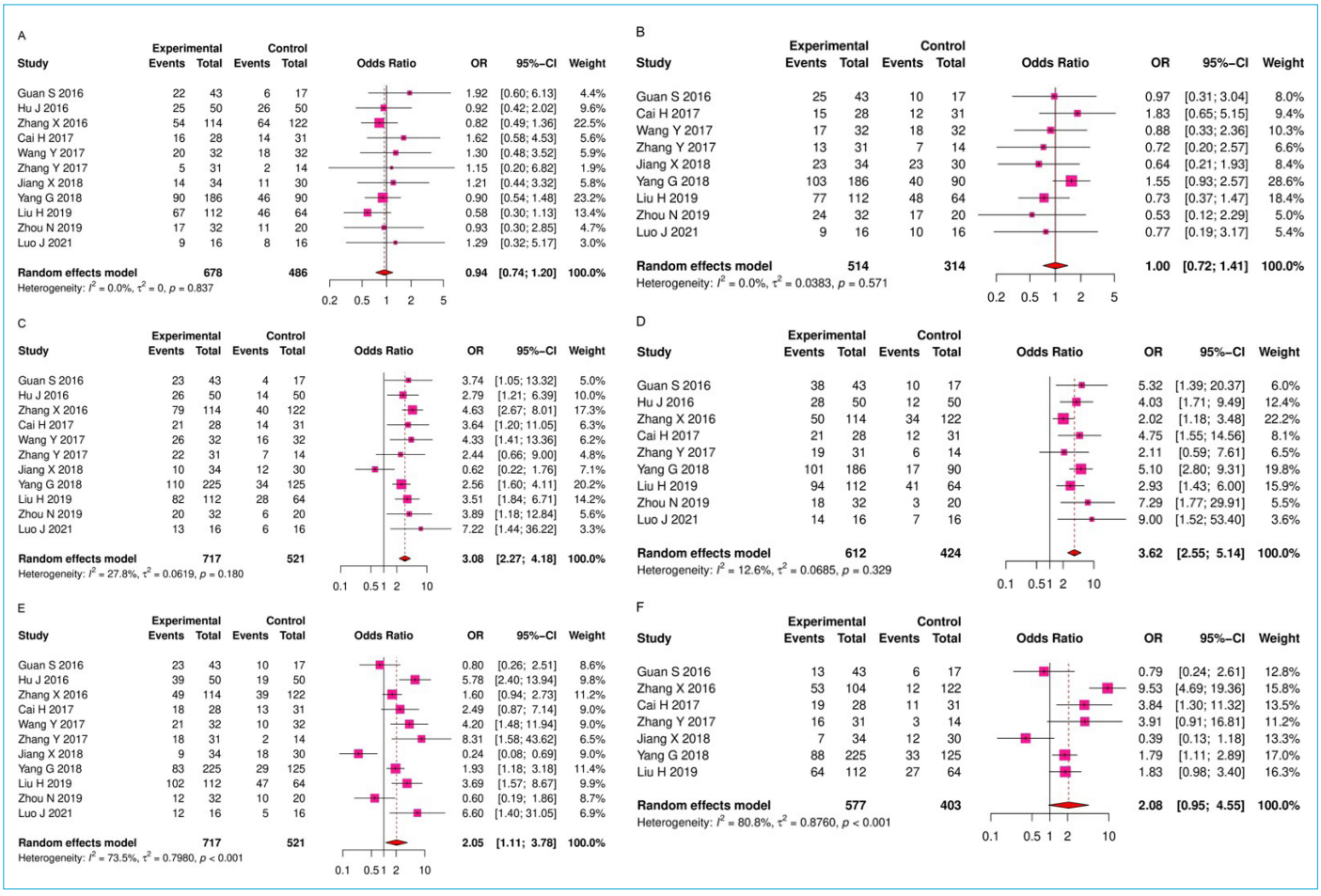

Figure 4. Association of low miR-613 levels with old age **(a)**, male gender **(b)**, advanced disease staging **(c)**, lymph-node metastasis **(d)**, larger tumor size **(e)**, and poor tumor differentiation **(f)**.

world. The non-invasive approach also allows us to evaluate the prognostic role of miR-613 adequately because it is not certain that miR-613 expression levels in the blood are matched directly to tissue samples. Moreover, We still do not know whether using a single or both types of samples will be best. Secondly, future studies should be done globally other than Asian ethnicities due to the certain genetic variations between populations.[33] Thirdly, prognostic assessments on other specific regimens such as chemotherapy, radiotherapy, and targeted therapies are encouraged. In that trials, a multivariate analysis model combined miR-613 with other diagnostic tests and clinical features should be applied, which were less observed in this meta-analysis.[13,16,22,24] Finally, standardization of the RT-qPCR technique used in detecting miR-613 is requested to increase reproducibility between centers. Such variables may include time and conditions of sample storage, processing, extraction method, normalization gene, and cut-off value.[34] For example, experts recommended using miR-16 and miR-103a as endogenous normalization control alternatives to U6 in the RT-qPCR reactions.[35,36]

Conclusion

In conclusion, this meta-analysis indicates that low expression of miR-613 in tissue samples is associated with advanced disease staging, larger tumor size, and lymph node metastasis in cancers. Importantly, low miR-613 is a poor prognosis factor for PFS and OS, enabling its clinical usage near future.

Disclosures

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – T.T.P., S.T.N.; Design – T.T.P., S.T.N., T.T.N.; Supervision – T.T.P., S.T.N., T.T.N.; Materials – S.T.N., T.T.N.; Data collection &/or processing – V.T.T., T.T.P., K.Q.H., T.T.H., S.P.P., H.T.N., H.D.T., L.T.N., T.H.P., B.T.L.; Analysis and/or interpretation – V.T.T., T.T.P., K.Q.H.; Literature search – T.T.P., S.T.N.; Writing – V.T.T., T.T.P., K.Q.H.; Critical review – S.T.N., T.T.N.

References

1. Allemani C, Matsuda T, Carlo VD, Harewood R, Matz M, Nikšić M, et al. Global surveillance of trends in cancer survival 2000-

14 (CONCORD-3): Analysis of individual records for 37,513,025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet 2018;391:1023–75.
2. Fu Z, Wang L, Li S, Chen F, Au-Yeung KK, Shi C. MicroRNA as an important target for anticancer drug development. Front Pharmacol 2021;12:736323.
3. Mei J, Xu R, Hao L, Zhang Y. MicroRNA-613: A novel tumor suppressor in human cancers. Biomed Pharmacother 2020;123:109799.
4. Yan Z, Yin H, Lin G. CircDDX42 accelerates the development of pancreatic cancer via miR-613/ID4/PI3K/AKT axis. Onco Targets Ther 2020;13:10945–57.
5. Duan W, Pan S, Zhai Y, Deng Q, Ren W, Du C, et al. miR-613 suppresses renal cell carcinoma proliferation, invasion and migration by regulating the AXL/AKT pathway. Exp Biol Med 2023;248:281–92.
6. Hu G, Ma J, Zhang J, Chen Y, Liu H, Huang Y, et al. Hypoxia-induced lncHILAR promotes renal cancer metastasis via ceRNA for the miR-613/206/1-1-3p/Jagged-1/Notch/CXCR4 signaling pathway. Mol Ther 2021;29:2979–94.
7. Deng L, Yin Q, Liu S, Luo D. MicroRNA-613 enhances nasopharyngeal carcinoma cell radiosensitivity via the DNA methyltransferase 3B/tissue inhibitor of matrix metalloproteinase-3/signal transducer and activator of transcription-1/forkhead box O-1 axis. Dis Markers 2022;2022:5699275.
8. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. PLoS Med 2021;18:e1003583.
9. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Available at: https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed Dec 13, 2023.
10. Tierney JF, Stewart LA, Ghersi D, Burdett S, Sydes MR. Practical methods for incorporating summary time-to-event data into meta-analysis. Trials 2007;8:16.
11. Harrer M, Cuijpers P, Furukawa TA, Ebert DD. Doing meta-analysis with R: A hands-on guide. London: CRC Press; 2021.
12. Shim SR, Kim SJ, Lee J. Diagnostic test accuracy: Application and practice using R software. Epidemiol Health 2019;41:e2019007.
13. Guan S, Wang C, Chen X, Liu B, Tan B, Liu F, et al. MiR-613: A novel diagnostic and prognostic biomarker for patients with esophageal squamous cell carcinoma. Tumour Biol 2016;37:4383–91.
14. Hu J, Qin C, Gao Y, Zhang X, Zhang M, Lu Y. MicroRNA-613 suppresses colon cancer proliferation via targeting neurokinin-1. Int J Clin Exp Pathol 2016;9:12511–18.
15. Li D, Li DQ, Liu D, Tang XJ. MiR-613 induces cell cycle arrest by targeting CDK4 in non-small cell lung cancer. Cell Oncol 2016;39:139–47.
16. Zhang X, Zhang H. Diminished miR-613 expression as a novel prognostic biomarker for human ovarian cancer. Eur Rev Med Pharmacol Sci 2016;20:837–41.
17. Cai H, Yao J, An Y, Chen X, Chen W, Wu D, et al. LncRNA HOTAIR acts as competing endogenous RNA to control the expression of Notch3 via sponging miR-613 in pancreatic cancer. Oncotarget 2017;8:32905–17.
18. Wang Y, Zhao P, Qian D, Hu M, Zhang L, Shi H, et al. MicroRNA-613 is downregulated in HCMV-positive glioblastoma and inhibits tumour progression by targeting arginase-2. Tumour Biol 2017;39:1010428317712512.
19. Zhang Y, Zhu X, Zhu X, Wu Y, Liu Y, Yao B, et al. MiR-613 suppresses retinoblastoma cell proliferation, invasion, and tumor formation by targeting E2F5. Tumour Biol 2017;39:1010428317691674.
20. Jiang X, Wu J, Zhang Y, Wang S, Yu X, Li R, et al. MiR-613 functions as tumor suppressor in hepatocellular carcinoma by targeting YWHAZ. Gene 2018;659:168–74.
21. Sang Q, Liu X, Sun D. Role of miR-613 as a tumor suppressor in glioma cells by targeting SOX9. Onco Targets Ther 2018;11:2429–38.
22. Yang G, Fu Y, Lu X, Wang M, Dong H, Li Q. LncRNA HOTAIR/miR-613/c-met axis modulated epithelial-mesenchymal transition of retinoblastoma cells. J Cell Mol Med 2018;22:5083–96.
23. Zhu Y, Tang L, Zhao S, Sun B, Cheng L, Tang Y, et al. CXCR4-mediated osteosarcoma growth and pulmonary metastasis is suppressed by MicroRNA-613. Cancer Sci 2018;109:2412–22.
24. Liu H, Chen K, Wang L, Zeng X, Huang Z, Li M, et al. miR-613 inhibits Warburg effect in gastric cancer by targeting PFKFB2. Biochem Biophys Res Commun 2019;515:37–43.
25. Zhou N, He Z, Tang H, Jiang B, Cheng W. LncRNA RMRP/miR-613 axis is associated with poor prognosis and enhances the tumorigenesis of hepatocellular carcinoma by impacting oncogenic phenotypes. Am J Transl Res 2019;11:2801–15.
26. Luo J, Jin Y, Li M, Dong L. Tumor suppressor miR 613 induces cisplatin sensitivity in non small cell lung cancer cells by targeting GJA1. Mol Med Rep 2021;23:385.
27. Su Y, Liang C, Yang Q. LncRNA MALAT1 promotes glioma cell growth through sponge miR-613. JBUON 2021;26:984–91.
28. Yao Q, Zhang L, Wang Y, Liu J, Yang L, Wang Y. LncRNA UCA1 elevates the resistance of human leukemia cells to daunorubicin by the PI3K/AKT pathway via sponging miR-613. Biosci Rep 2021;41:BSR20201389.
29. Wang Y, Xin D, Zhou L. LncRNA LINC00152 increases the aggressiveness of human retinoblastoma and enhances carboplatin and adriamycin resistance by regulating MiR-613/Yes-associated protein 1 (YAP1) axis. Med Sci Monit 2020;26:e920886.
30. Wang L, Chen X, Sun X, Suo J. Long noncoding RNA LINC00460

facilitates colorectal cancer progression by negatively regulating miR-613. Onco Targets Ther 2020;13:7555–69.
31. Li B, Liu D, Yang P, Li HY, Wang D. miR-613 inhibits liver cancer stem cell expansion by regulating SOX9 pathway. Gene 2019;707:78–85.
32. Liu C, Jiang F, Zhang X, Xu X. Long non-coding RNA UCA1 modulates paclitaxel resistance in breast cancer via miR-613/CDK12 axis. Cancer Manag Res 2020;12:2777–88.
33. Rawlings-Goss RA, Campbell MC, Tishkoff SA. Global population-specific variation in miRNA associated with cancer risk and clinical biomarkers. BMC Med Genomics 2014;7:53.
34. Khan J, Lieberman JA, Lockwood CM. Variability in, variability out: Best practice recommendations to standardize preanalytical variables in the detection of circulating and tissue microRNAs. Clin Chem Lab Med 2017;55:608–21.
35. Xiang M, Zeng Y, Yang R, Xu H, Chen Z, Zhong J, et al. U6 is not a suitable endogenous control for the quantification of circulating microRNAs. Biochem Biophys Res Commun 2014;454:210–4.
36. Veryaskina YA, Titov SE, Zhimulev IF. Reference genes for qPCR-based miRNA expression profiling in 14 human tissues. Med Princ Pract 2022;31:322–32.