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Review

Prognostic value of microRNA-155 in human carcinomas: An updated meta-analysis

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ABSTRACT

Background: miR-155 functions as an oncomiR or as an oncosuppressor-miR in human cancer. Although miR-155 has been researched in many cancers, its prognostic value is uncertain.
Methods: We performed a literature search in up-to-date electronic databases including PubMed and Embase to obtain as many relevant articles as possible. Combined hazard ratios (HR) of miR-155 for outcome were analyzed.
Results: A total of 24 papers researching different cancers were included in this meta-analysis. Combined HRs showed that miR-155 was significantly associated with a poorer OS with HR = 1.99 (1.34–2.96) (I-squared = 83.1%, $P = 0.000$). Combined HR of PFS/RFS/DFS was 1.95 (1.14–3.33) (I-squared = 75.9%, $P = 0.000$) and CSS/DSS was 2.50 (0.73–8.58) (I-squared = 87.7%, P = 0.000).
Conclusion: Increased miR-155 expression was associated with poorer survival in human carcinoma and as such may be valuable in predicting outcome.

1. Introduction

MicroRNAs, a class of 21–23 nucleotide single-stranded and highly conserved non-coding RNAs, were found to have crucial roles in cellular processes including differentiation, proliferation, apoptosis and stress response [1]. Additionally, they appear to be pivotal regulators of many diseases including neurologic disorders, heart disease, vascular diseases, and especially cancer [2]. MicroRNAs regulate molecular pathways in cancer by targeting various oncogenes and tumor suppressors [3]. In humans, miR-155, located on chromosome 21, was identified initially as a frequent integration site in lymphoma [4]. Studies have found that miR-155 functioned as an oncomiR or as an oncosuppressor-miR in human cancer. For example, miR-155 promoted progression of hepatocellular, breast, bladder, colon cancer, etc. [5–8] It was also reported that miR-155 functioned as a suppressor in ovarian and gastric cancer, among others [9,10]. Although miR-155 typically functioned as an oncomiR in many tumors, its exact role remains inconclusive.

The clinical value of miR-155 has been researched in many carcinomas. Aberrant expression of miR-155 was of potential diagnostic value of several types of cancers, such as colorectal lung and breast cancer [11–13]. In recent years, the prognostic value of miR-155 has been studied in many diseases. Unfortunately, results were largely inconclusive and sometimes contradictory. For example, increased miR-155 was associated with poorer survival in cervical cancer and oral squamous cell carcinoma [14,15]. In contrast, some studies found that miR-155 predicted prognosis in pancreatic cancer [16]. In this study, we carried out a systematical review and meta-analysis to evaluate the prognostic value of miR-155 in cancer based on current published studies.

2. Methods

2.1. Search strategy of published papers

The purpose of our study was to investigate the association between the miR-155 and prognosis in different tumors. We performed a literature search in up-to-date electronic databases, including PubMed and Embase, to obtain as many relevant articles as possible. The process was completed by two workers. The literature search ended in June 10, 2017. We searched with key aspects, “miR-155” and “cancer”. The details were as follows: (“microRNA 155” OR “miR 155” OR “miR-155” OR “miRNA” OR “miRNAs”) AND (“cancer” OR “cancers” OR “tumor”

Abbreviations: OS, overall survival; CSS, cancer-special survival; DSS, disease-special survival; DFS, disease-free survival; RFS, recurrence -free survival; PFS, progression-free survival; HR, hazard ratio; CI, confidence interval

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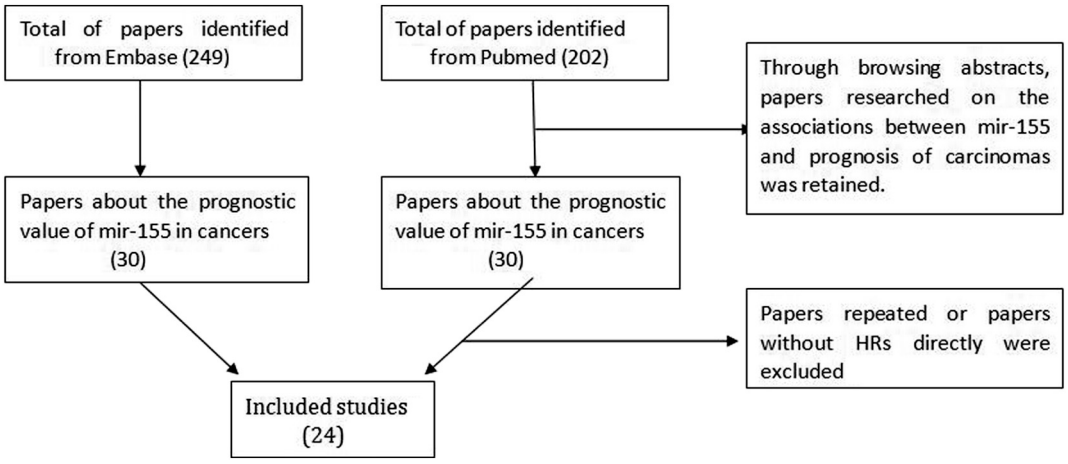

Fig. 1. Flow chart of study selection process.

Table 1
The characters of included 24 studies.

Studies	Countries	Members	Design style	Cancer	Survivals	HR (95%CI)	P value	MicroRNA assay	Origins	Follow-up
Jang MH (2017)	Korean	190	R	Breast cancer	PFS	2.824(1.265–6.304)	0.011	qRT-PCR	Tumor	66(2.4–155)
HuiFang (2016)	Chinese	129	P	Cervical cancer	OS	2.320(1.259–4.276)	0.007	qRT-PCR	Tumor	60
Osamu (2016)	Japan	73	p	OSCC	OS	5.156(1.253–21.202)	0.023	qRT-PCR	Tumor	24(3–50)
Xin Zhang (2016)	Chinese	162	P	Bladder cancer	RFS PFS	3.497 (1.722–7.099) 9.466(1.210–74.066)	0.001 0.032	qRT-PCR	Urine	51(6–65)
Shi LJ (2015)	Chinese	30	P	OSCC	OS	6.986 (1.684–28.997)	0.007	qRT-PCR FISH	Tumor	32(5–50)
Wang H (2015)	Chinese	102	P	Bladder cancer	PFS	7.7 (1.4–14.7)	0.009	qRT-PCR	Tumor	60
Lv ZC (2015)	Chinese	146	P	Colorectal cancer	OS PFS	3.864 (1.522–8.665) 2.554 (1.258–6.543)	0.003 0.008	qRT-PCR	Serum	57(6–76)
Zhang XL (2015)	Chinese	133	R	Gallbladder cancer	OS	2.394 (1.568–10.034)	0.009	qRT-PCR	Tumor	60
Yi GAO (2014)	Chinese	162	R	NSCLC	OS	2.311 (1.479–3.611)	0.000	qRT-PCR	Tumor	14.5
Kono H (2013)	Japan	56	P	Gallbladder cancer	DSS	9.9 (1.10–29.4)	0.03	qRT-PCR	Tumor	45
Shinmei S (2013)	Japan	137	P	Renal cancer	DSS	5.49 (2.40–12.52)	0.0001	qRT-PCR	Tumor	65(2–188)
Sanfiorenzo C (2013)	France	52	P	NSCLC	DFS	0.060 (0.005–0.767)	0.030	qRT-PCR	Serum	46
Papaconstantinou IG (2013)	Greece	88	P	PADC	OS	0.3181 (0.11–0.92)	0.04	qRT-PCR	Tumor	78
Song CG (2012)	Chinese	88	P	Breast cancer	OS	1.58 (0.87–3.16)	0.082	qRT-PCR	Tumor	60
Chen J (2012)	Chinese	92	P	Breast cancer	OS	2.781 (2.135–4.902)	0.009	qRT-PCR	Tumor	60
Huang YH (2012)	Chinese	216	R	HCC	OS RFS	0.823 (0.394–1.719) 1.577 (1.097–2.266)	0.6 0.013	qRT-PCR	Tumor	120
Han ZB (2012)	Chinese	100	P	HCC	OS RFS	4.736 (2.332–9.619) 2.748 (1.277–5.914)	0.001 0.01	qRT-PCR	Tumor	100
Saito M (2011)	USA	89	R	NSCLC	CSS	2.37 (1.27–4.42)	0.006	qRT-PCR	Tumor	80
Donnem T (2011)	Norway	335	P	NSCLC	CSS	0.45 (0.21–0.96) 1.87 (1.01–3.48)	0.039 0.047	ISH	Tumor	86(48–216)
Voortman,J (2011)	USA	639	P	NSCLC	OS	0.91 (0.72;1.13)	0.09	qRT-PCR ISH	Tumor	96
Rossi S (2010)	USA	104	P	CLL	OS DFS	2.00 (0.90, 4.41) 1.36 (0.65, 2.86)	0.089	qRT-PCR	Serum	20(0–88)
Greither T (2010)	Germany	56	P	PADC	OS	2.50 (1.32, 4.74)	0.005	qRT-PCR	Tumor	16(1–61)
Shibuya H (2010)	Japan	156	P	Colorectal cancer	OS DFS	0.427 (0.223–0.838) 0.387 (0.179–0.872)	0.014 0.023	qRT-PCR	Tumor	44(2–84)
Yanaihara N (2006)	USA	55	P	Lung cancer	OS	3.03 (1.13–8.14)	0.027	qRT-PCR	Tumor	60