

## Supplementary File

**Table S1.** Methodology of miRNA analysis and study outcomes for lymph node metastases

<b>Study</b>	<b>Country</b>	<b>LNM/non-LNM</b>	<b>Specimen</b>	<b>Methodology</b>	<b>Outcome</b>	<b>Statistics</b>
Chou et al. [15]	Taiwan	37/63	FF	Microarray, qRT-PTC	Different miRNA expression levels according to LNM status	Mann-Whitney U
Yu et al. [17]	China	60/49 (serum)	Serum, FFPE	Solexa, qRT-PCR	Different miRNA expression levels according to LNM status, correlation between serum and tissue miRNA levels	One-way ANOVA, Pearson's correlation coefficient
Zhou et al. [18]	China	39/12 (BRAF+ 23/3, BRAF- 16/9)	FF	Northern blot	Different miRNA expression levels according to LNM status	Mann-Whitney U
Sun et al. [19]	China	29/23	FFPE	qRT-PCR	Different miRNA expression levels according to LNM status	Mann-Whitney U
Wang et al. [20]	China	52/39	FF	microarray, qRT-PTC	Different miRNA expression levels according to LNM status	Mann-Whitney U

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Wang et al. [21]	China	51/36 (LNM+/-), 28/23 (CLN/LLN)	FF	microarray, qRT-PTC	Different miRNA expression levels according to LNM status	Student's t (LNM+/-), Mann-Whitney U (CLN/LLN)
Peng et al. [22]	China	21/15	FF	microarray, qRT-PTC	Different miRNA expression levels according to LNM status	Kruskal-Wallis H
Lee et al. [23]	South Korea	45/25	Plasma	qRT-PCR	Different miRNA expression levels according to LNM status	Mann-Whitney U
Acibucu et al. [24]	Turkey	16/41	FFPE	qRT-PCR	Different miRNA expression levels according to LNM status	Student's t
Sun et al. [25]	China	39/89	FF, blood	qRT-PCR	Different miRNA expression levels according to LNM status	Student's t
Han et al. [26]	USA	101/136	FFPE	qRT-PCR	Association of miRNA and LNM, independent predictors for LNM	Univariate, multivariate logistic regression
Hu et al. [27]	China	90/176	FF, plasma	qRT-PCR	Different miRNA expression levels according to LNM status	Student-T

<b>Study</b>	<b>Country</b>	<b>LNM/non-LNM</b>	<b>Specimen</b>	<b>Methodology</b>	<b>Outcome</b>	<b>Statistics</b>
Liu et al. [28]	China	69/62	FFPE	qRT-PCR	Difference in expression of high/low miRNA groups between LNM+/-	Chi-square
Huang et al. [29]	China	41/46	Serum	qRT-PCR	Difference in expression of high/low miRNA groups (based on median value) between LNM+/-	Chi-square
Ren et al. [30]	China	22/62	Serum	qRT-PCR	Difference in expression of high/low miRNA groups (based on mean value) between LNM+/-	Chi-square
Liu et al. [31]	China	110/26	FF	qRT-PCR	Difference in expression of high/low miRNA groups between LNM+/- groups	Chi-square
Zhang et al. [32]	China	9/45 (FFPE), 18/52 (Serum)	FFPE, serum	qRT-PCR	Different miRNA expression levels according to LNM status, diagnostic utility of miRNA in predicting LNM	Mann-Whitney U, ROC (serum, FFPE)

<b>Study</b>	<b>Country</b>	<b>LNM/non-LNM</b>	<b>Specimen</b>	<b>Methodology</b>	<b>Outcome</b>	<b>Statistics</b>
Todorovic et al. [33]	Serbia	10/26	FF	qRT-PCR	Association of miRNA and LNM	Univariate by Mann-Whitney U, multivariate logistic regression
Yang et al. [34]	China	187/59	FNA	qRT-PCR	Different miRNA expression levels according to LNM status	Mann-Whitney U
Todorovic et al. [35]	Serbia	11/31	FF	qRT-PCR	Different miRNA expression levels according to LNM status	Mann-Whitney U
Xiang et al. [36]	China	67/23 (CLN+/-), 31/59 (LLN+/-)	FFPE	qRT-PCR	Different miRNA expression levels according to LNM status	Mann-Whitney U
Yao et al. [37]	China	47/104	FF	qRT-PCR	Difference in expression of high/low miRNA groups (based on median value) between LNM+/- groups	Chi-square
Jiang et al. [38]	China	49/15	Plasma exosomes	qRT-PCR	Different miRNA expression levels according to LNM status, predictive factors for	Student's t, Cox, ROC

Study	Country	LNM/non-LNM	Specimen	Methodology	Outcome	Statistics
Dai et al. [39]	China	52/44	Plasma and serum exosomes	qRT-PCR	LNM, diagnostic utility of miRNA in predicting LNM Different miRNA expression levels according to LNM status, diagnostic utility of miR in predicting LNM	Mann-Whitney U, ROC
Pamedytyte et al. [40]	Lithuania	91/309	FFPE	qRT-PCR	Different miRNA expression levels according to LNM status	Student's t
Liu et al. [41]	China	35/65	FFPE, plasma	qRT-PCR	Different miRNA expression levels according to LNM status, diagnostic utility of miRNA in predicting LNM	Student's t, ROC (plasma)
Shi et al. [16]	China	32/19 (CLN +/-), 17/34 (LLN +/-)	Tissue	qRT-PCR	Difference in expression of high/low miRNA groups (based on mean value) between CLN+/- and LLN+/- groups	Chi-square

FF — freshly frozen (snap-frozen); FFPE — formalin-fixed paraffin-embedded; FNA — fine-needle aspiration; qRT-PCR — quantified real-time polymerase chain reaction; CLN — central lymph node metastases; LLN — lateral lymph node metastases



**Table S2.** Summary of risk of bias by QUADAS-2 methodology

Study	Risk of bias				Applicability concerns			
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard	
Chou et al. [15]	Low	Low	Low	Low	Low	High	Low	
Yu et al. [17]	Low	Low	Low	Low	Low	Low	Low	
Zhou et al. [18]	Low	Low	Low	Low	Low	High	Low	
Sun et al. [19]	Unclear	Low	Low	Low	Low	High	Low	
Wang et al. [20]	Low	Low	Low	Low	Low	High	Low	
Wang et al. [21]	Low	Low	Low	Low	Low	High	Low	
Peng et al. [22]	Low	Low	Low	Low	Low	High	Low	
Lee et al. [23]	Low	Low	Low	Low	Low	Low	Low	
Acibueu et al. [24]	Unclear	Low	Low	Low	Low	High	Low	
Sun et al. [25]	Low	Low	Low	Low	Low	Low	Low	
Han et al. [26]	Low	Low	Low	Low	Low	Low	Low	
Hu et al. [27]	Low	Low	Low	Low	Low	Low	Low	
Liu et al. [28]	Low	Low	Low	Low	Low	High	Low	
Huang et al. [29]	Low	Low	Low	Low	Low	Low	Low	
Ren et al. [30]	Low	Low	Low	Low	Low	Low	Low	
Liu et al. [31]	Low	Low	Low	Low	Low	High	Low	
Zhang et al. [32]	Low	Low	Low	Low	Low	High	Low	

Study	Risk of bias						Applicability concerns			
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard			
Todorovic et al. [33]	Low	Low	Low	Low	Low	High	Low	Low	Low	Low
Yang et al. [34]	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Todorovic et al. [35]	Low	Low	Low	Low	Low	High	Low	Low	Low	Low
Xiang et al. [36]	Low	Low	Low	Low	Low	High	Low	Low	Low	Low
Yao et al. [37]	Low	Low	Low	Low	Low	High	Low	Low	Low	Low
Jiang et al. [38]	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Dai et al. [39]	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Pamedytyte et al. [40]	Low	Low	Low	Low	Low	High	Low	Low	Low	Low
Liu et al. [41]	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Shi et al. [16]	Low	Unclear	Low	Low	Low	High	Low	Low	Low	Low



**Table S3.** miRNA changes associated with lymph node metastasis (LNM)

Study	↑miRNA	↓ miRNA	No statistically significant difference
Chou et al. [15]			miR-221, miR-222, miR-146b
<b>Yu et al.</b> [17]	<b>miR-151-5p<sup>1</sup>, miR-222<sup>1</sup></b>		<b>miR-let7e<sup>2</sup></b>
Zhou et al. [18]	miR-221 (all PTC, BRAF+)		miR-221 (BRAF-)
Sun et al. [19]	miR-221, miR-222		miR-146b, miR-181, miR-21
Wang et al. [20]			miR-146b, miR-221, miR-222, miR-135b
Wang et al. [21]	miR-2861, miR-451 (LNM+/-, LLN/CLN groups)		
Peng et al. [22]	miR-199b-5p		miR-30a-3p, miR-146b-5p
<b>Lee et al.</b> [23]			<b>miR-221, miR-222, miR-146b, miR-155 (LNM+/-, LLN/CLN)</b>
Acibucu et al. [24]	miR-221, miR-222, miR-146b		
<b>Sun et al.</b> [25]	miR-146a		<b>miR-146a, miR-146b (blood and tissue)</b>
Han et al. [26]	miR-146b-5p <sup>3,4,5</sup> , miR-221 <sup>3</sup> , miR-222 <sup>3,5</sup> , miR-146b-3p <sup>4,5</sup>		miR-21, miR-204, miR-221 <sup>4,5</sup> , miR-375
<b>Hu et al.</b> [27]		miR-940, miR-15a, miR-16	<b>miR-940, miR-15a, miR-16</b>
Liu et al. [28]		miR-let7a	
<b>Huang et al.</b> [29]		<b>miR-381</b>	

Study	↑ miRNA	↓ miRNA	No statistically significant difference
Ren et al. [30]		miR-26a	
Liu et al. [31]		miR-199a-3p	
Zhang et al. [32]		miR-451 (serum and tissue)	
Todorovic et al. [33]	miR-92a <sup>3,4</sup>		
Yang et al. [34]	miR-146b		
Todorovic et al. [35]			miR-30a-3p
Xiang et al. [36]	miR-222 (CLN+/-, LLN +/-)		miR-222 (CLN+/LLN+)
Yao et al. [37]	miR-182		
Jiang et al. [38]	miR-21-5p, miR-146b-5p <sup>6</sup> , miR-204-5p, miR-221-3p, and miR-222-3p <sup>6</sup> .		miR-451a, miR-7-5p, miR-30a-3p, miR-138-5p, miR-199a-3p.
Dai et al. [39]	miR-485-3p, miR-4433a-5p		miR-204-3p, miR-376a-3p, miR-4306-5p.
Pamedytyte et al. [40]	miR-146b, miR-222, miR-21, miR-221, miR-181b		
Liu et al. [41]	miR-323 (plasma and tissue)		
Shi et al. [16]		miR-9	

**bold** — specimens obtained preoperatively; miR — microRNA; PTC — papillary thyroid carcinoma; LNM — lymph node metastasis; CLN — central cervical lymph node metastasis; LLN — lateral cervical lymph node metastasis; <sup>1</sup>additionally serum and tissue levels of these miR correlated, and serum levels decreased after surgery; <sup>2</sup>additionally no significant correlation between serum and tissue level, and serum level did not decrease after surgery; <sup>3</sup>in univariate analysis; <sup>4</sup>in multivariate analysis; <sup>5</sup>in multivariate analysis with preoperative information; <sup>6</sup>independent risk factors for LNM