

Circulating miRNA-based biomarkers of ischemic stroke recovery

Table S3-Correlational analysis of biomarkers associated with different recovery assessment scores

Author + Year (+ref)	miRNA	miRNA source	miRNA collection time	Correlation coefficient (Spearman unless specified)	Sample size	Disability scale	Disability score timing	Observations
Ma et al, 2022 [1]	EMVs	Plasma	<24 h	0.341	72	NIHSS	At admission (within 24 h)	Pearson r Opposite correlations for total EMVs and miR-125a-5p-loaded EMVs
	miR-125a-5p-loaded EMVs			-0.276	72	NIHSS		
Peng et al., 2015 [2]	miR-let-7e	Serum	<24 h	0.29 (NS)	72	NIHSS	At admission (within 24 h)	
Wu et al., 2017 [3]	miR-23b-3p	Serum	<24 h	0.190	227	NIHSS	At admission (within 24 h)	
				0.178		mRS	At discharge (within 12 days)	
				-0.232		BI	At discharge (within 12 days)	
	miR-29b-3p	Serum	<24 h	0.181	227	NIHSS	At admission (within 24 h)	
				-0.187		BI	At discharge (within 12 days)	
	miR-181a-5p	Serum	<24 h	0.412	227	NIHSS	At admission (within 24 h)	
	miR-21-5p	Serum	<24 h	0.268	227	NIHSS	At admission (within 24 h)	
	miR-125a-5p	Serum	<72 h after central vertigo occurrence due to AIS	0.239 (NS)	23	NIHSS	At admission (within 72 h)	Posterior circulation stroke Patients with central vertigo due to acute stroke
Kijpaaisalratana et al. 2020 [4]	miR-125b-5p	Serum		-0.006 (NS)		NIHSS	At admission (within 72 h)	
	miR-433-5p	Serum		0.085 (NS)		NIHSS	At admission (within 72 h)	

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Kautzky et al., 2022 [5]	miR-125b-5p	Plasma	On admission	0.39 0.56	40	NIHSS mRS	Day 2 Day 7	Kendall τ
Zhu et al., 2019 [6]	miR-143	PBMC	< 24 h	0.203	170	NIHSS	At admission (within 24 h)	
Niu et al., 2021 [7]	miR-369-3p	Plasma	<72 h	-0.021 (NS)	453	NIHSS	At admission (within 72 h)	Exosomal
	miR-493-3p	Plasma	<72 h	-0.183	453	NIHSS	At admission (within 72 h)	Exosomal
	and miR-379-5p	Plasma	<72 h	-0.068 (NS)	453	NIHSS	At admission (within 72 h)	Exosomal
	miR-1296-5p	Plasma	<72 h	-0.185	453	NIHSS	At admission (within 72 h)	Exosomal
Li et al., 2022 [8]	miR-29b	Leukocytes	<6 h	-0.491	50	NIHSS	At admission (within 6 h)	Pearson r Anterior circulation stroke
Kotb et al., 2019 [9]	miR-146a	Serum	<24 h	-0.352	44	GCS	At admission (within 24 h)	Comatose patients with severe AIS
Wu et al., 2020 [10]	miR-99b	Plasma	Unclear	-0.56	112	GOS	at day 30	-
Huang et al., 2016 [11]	miR-132	Serum	chronic	-0.859	76	MoCA	chronic	
Zhai et al., 2020 [12]	miR-195	Serum	At admission (within 72 hours)	0.655	108	NIHSS	At admission (within 72 hours)	-
				-0.773		MoCA		
	miR-497	Serum		0.652		NIHSS		
Ma et al., 2019 [13]				-0.773		MoCA		
	miR-93	Neutrophils and plasma	< 6 h	0.4124	33	BI (p=0.0211)	At admission (<6 h) + 7 days after stroke onset	miR-93 expression in plasma correlates with expression in neutrophils

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Lin et al., 2022 [14]	miR-411-5p	Serum	before rt-PA, 24 h after rt-PA, and 3 months (90 days) after stroke onset	-0.470	96	NIHSS	at 24 h after thrombolysis	Correlation between miR-411-5p expression and NIHSS after thrombolysis
Xiang et al. 2017 [15]	let-7i	plasma	24 h after thrombolysis	0.28	40	NIHSS	at diagnosis	Pearson r Thrombolysis Let-7i positively correlates with NIHSS score after thrombolysis
Wang et al. 2020 [16]	let-7i	serum	Chronic (within 1 year)	0.643	36	MoCA	chronic (within 1 year)	Correlation sample included both PSCI and Non-PSCI patients
Jickling et al. 2016 [17]	let-7i	circulating leukocytes	<72h	-0.38	106	NIHSS	at diagnosis	Pearson r
Wang et al. 2019 [18]	miR-124	serum	unclear	0.374	80	NIHSS	at diagnosis (within 24 h after stroke onset)	Correlation sample included both patients and controls
Yuan et al. 2022 [19]	miR-21	serum	14 days	0.752	77	MMSE	14 days	
	miR-132	serum	14 days	0.319	77	MMSE	14 days	
	miR-200b	serum	14 days	0.379	77	MMSE	14 days	
Zhou and Qi 2021 [20]	miR-124	serum	24, 48, 72 h	0.5932	108	GOS	30 days	
Ji et al. 2016 [21]	miR-124	serum	mean 16.5 h	0.6825	65	NIHSS	at diagnosis	Exosomal
	miR-9	serum	mean 16.5 h	0.7126	65	NIHSS	at diagnosis	Exosomal
He et al.	miR-124-3p	plasma	24 h after thrombolysis	0.382	84	NIHSS	at diagnosis	Thrombolysis

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2019 [22]	miR-125b-5p	plasma	24 h after thrombolysis	0.343	84	NIHSS	at diagnosis	Thrombolysis
He et al. 2019 [23]	miR-125b-5p	plasma	24 h after thrombolysis	0.262	94	NIHSS	On admission, at 24 h, on day 7	Thrombolysis
	miR-206	plasma	24 h after thrombolysis	0.341	94	NIHSS	On admission, at 24 h, on day 7	Thrombolysis miR-206 positively correlates with NIHSS scores on day 7 after thrombolysis
Qi et al. 2021 [24]	miR-124-3p	serum	2, 4, 6 h	-0.74	20	NIHSS	at diagnosis	Pearson r exosomal
Jin and Xing 2018 [25]	miR-126	plasma	<24 h	-0.402	148	NIHSS	at diagnosis	Probable patient overlap with Jin and Xing 2017 [26]
	miR-218	plasma	<24 h	0.471	148	NIHSS	at diagnosis	
	miR-130a	plasma	<24 h	-0.161 (NS)	148	NIHSS	At diagnosis	
	miR-185	plasma	<24 h	-0.129 (NS)	148	NIHSS	At diagnosis	
	miR-222	plasma	<24 h	-0.062 (NS)	148	NIHSS	At diagnosis	
Jin and Xing 2017 [26]	miR-126	plasma	<24 h	-0.398	106	NIHSS	at diagnosis	After thrombolysis
	miR-222	plasma	<24 h	0.698	106	NIHSS	at diagnosis	After thrombolysis
	miR-19a	plasma	<24 h	-0.026 (NS)	106	NIHSS	At diagnosis	After thrombolysis
	miR-296	plasma	<24 h	0.020 (NS)	106	NIHSS	At diagnosis	After thrombolysis
	miR-101	plasma	<24 h	-0.079 (NS)	106	NIHSS	At diagnosis	After thrombolysis
	miR-218	plasma	<24 h	0.099 (NS)	106	NIHSS	At diagnosis	After thrombolysis
	miR-206	plasma	<24 h	0.069 (NS)	106	NIHSS	At diagnosis	After thrombolysis
	miR-221	plasma	<24 h	0.033 (NS)	106	NIHSS	At diagnosis	After thrombolysis
	miR-378	plasma	<24 h	-0.557	106	NIHSS	at diagnosis	After thrombolysis

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	miR-185	plasma	<24 h	0.171 (NS)	106	NIHSS	at diagnosis	After thrombolysis
	miR-130a	plasma	<24 h	0.013 (NS)	106	NIHSS	at diagnosis	After thrombolysis
Chen et al. 2020 [27]	miR-195	plasma	<24 h	−0.139	215	NIHSS	at diagnosis	-
	miR-9	plasma	<24 h	−0.335	215	NIHSS	at diagnosis	
Yang et al. 2018 [28]	miR-195	plasma	<72 h	−0.3684	96	NIHSS	at diagnosis	
Liu et al. 2021 [29]	miR-21	PBMCs+serum	at diagnosis	−0.284	170	NIHSS	at diagnosis	
Zhou and Zhang 2014 [30]	miR-21	plasma	at diagnosis	−0.703	68	NIHSS	at diagnosis	
Wang et al. 2015 [31]	miR-29b	WBCs	<72 h	−0.349	58	NIHSS	at 3 months	
Ma et al. 2022 [32]	miR-29b	neutrophils	<6 h	−0.547	60	NIHSS	at diagnosis	
Abdelaleem et al. 2022 [33]	miR-9	serum	unclear	0.681	77	NIHSS	at diagnosis	Patients with stroke and type 2 diabetes
Xue et al. 2018 [34]	miR-9	serum	unclear	0.627	65	NIHSS	at diagnosis	
Xie et al. 2019 [35]	miR-124	plasma	unclear	−0.567	40	NIHSS	unclear	
	miR-24	Serum	unclear	−0.758	170	NIHSS	unclear	

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Guo et al., 2020 [36]	miR-29b	Serum	NA (abstract only)	-0.794	170	NIHSS	NA (abstract only)	Pearson r
Yuan et al., 2016 [37]	miR-335	Plasma	< 24 h following patient admission	-0.680	152	NIHSS	at admission	Pearson r Time from onset to admission <14 days
Yuan et al., 2016 [38]	miR-26b	Plasma	< 24 h following patient admission	-0.660	152	NIHSS	at admission	Pearson r Time from onset to admission <14 days
Zhao et al., 2016 [39]	miR-335	Plasma	< 24 h	-0.3682	168	NIHSS	At admission	Pearson r
Zhong et al., 2021 [40]	miR-497	Serum	At admission and at discharge	-0.611	128	NIHSS	At admission and clinical discharge	Intravenous thrombolysis or mechanical thrombectomy
Song et al., 2021 [41]	miR-409-3p	Serum	<9 h	0.865	80	NIHSS	Unclear	
Yang et al., 2020 [42]	miR-135b	Serum	< 24 h and at day 14 after stroke onset	-0.835	79	NIHSS	Unclear	
Liu et al., 2019 [43]	miR-128	Lymphocytes	< 72 h	0.3944	40	NIHSS	at 7 days	
				0.4357		mRS	at 90 days	
Zhao et al., 2020 [44]	miR-494	Lymphocytes	< 6h	0.3339	43	NIHSS	<6h	
Sheikhba haei et al., 2019 [45]	MiR-503	Serum	< 72 h + 3 months	0.45	50	NIHSS	< 72 h	Correlation sample included patients with diabetes and without stroke, diabetic patients with stroke, stroke patients without diabetes Higher disability at 3 months for patients
				0.48		acute phase mRS	< 72 h	

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								with higher initial expression of miR-503
Guo et al., 2022 [46]	miR-185	Serum	<24 h	0.735	142	NIHSS	<24h	
				0.802		mRS	<24h	
	miR-424	Serum	<24 h	0.796	142	NIHSS	<24h	
				0.873		mRS	<24h	
Fu et al., 2019 [47]	miR-451	Unknown	<12 hours	0.6104	108	NIHSS	3 months	
Ye et al., 2021 [48]	miRNA-27-3p	Serum	On hospital admission	0.7320	86	NIHSS	On hospital admission	Exosomal
Yang et al, 2016 [49]	miR-107	Plasma	<24 h	0.52	114	NIHSS	<24 h	
	miR-128b	Plasma	<24 h	0.44	114	NIHSS	<24 h	
	miR-153	Plasma	<24 h	0.35	114	NIHSS	<24 h	
Zhou et al., 2018 [50]	miR-134	Serum	at 24-, 48- and 72 h	0.6079	50	NIHSS	At admission (<24 h)	Exosomal
Chen et al., 2018 [51]	miR-146b	Serum	< 24 h	0.6460	128	NIHSS	at admission (<24 h) and 24 hours after stroke onset	
Chen et al., 2017 [52]	miR-223	Serum	< 72 h	0.31	50	NIHSS	at admission (<72 h)	Exosomal
Liang et al., 2016 [53]	mir-34a-5p	Plasma	< 12 h	-0.692	102	NIHSS	At admission	
Wang et al., 2014 [54]	miR-223	Leucocytes	At 24, 48, 72 h	-0.531	79	NIHSS	At admission (<72 h)	
	miR-9-5p	Serum	<6 h	0.066	88	mRS	At admission (<6 h)	

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Wang et al., 2021 [55]	miR-128-3p	Serum	<6 h	0.082	88	mRS	At admission (<6 h)
Jia et al., 2015 [56]	miR-145	Serum	<24 h	0.6288	146	NIHSS	At admission and 24 h after stroke onset
Liang et al., 2019 [57]	miR-140-5p	Plasma	<24 h	0.4625	62	HAMD	3 months
Hu et. al, 2020 [58]	miR-22	Plasma	< 7 days	0.635	73	HAMD	1 month
Cui et al., 2021 [59]	miR-221-3p	Serum	Chronic (unknown)	0.620	136	NIHSS	Chronic (unknown)
				0.608	136	HAMD	Chronic (unknown)

Notes: Jin and Xing 2018 is a follow-up study of Jin and Xing 2017, overlapping study periods, being performed in the same medical center and having very similar results ($I^2=0\%$). We presume that patients from the first study were included in the second. Studies with *unclear* miRNA collection timing do not explicitly state the timing of blood collection, but it is reasonable to presume that it was collected in the acute phase (i.e. within hours or days of hospital admission). Abbreviations: AIS, Acute ischemic stroke; BI, Barthel Index; EMVs, Endothelial Microvesicles; GCS, Glasgow Coma Scale; GOS, Glasgow Outcome Scale; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; miR, microRNAs; mRS, Modified Rankin score; NIHSS, National Institute Health Stroke Score

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