Am J Transl Res 2024;16(6):2711-2718
www.ajtr.org /ISSN:1943-8141/AJTR0156775

Original Article

Clinical implications of serum miR-34a in breast cancer and its predictive value for the efficacy of neoadjuvant chemotherapy

Yanyan Hong, Tingting Chen, Qian He, Qiang Ma, Zhendong Chen

Department of Oncology, The Second Affiliated Hospital of Anhui Medical University, Hefei 230601, Anhui, China

Received March 25, 2024; Accepted June 5, 2024; Epub June 15, 2024; Published June 30, 2024

Abstract: Objectives: This study aims to explore the implications of serum miR-34a in breast cancer (BC) and its predictive value for the efficacy of neoadjuvant chemotherapy (NACT). Methods: A retrospective analysis was performed on 102 female BC patients (research group) admitted to The Second Affiliated Hospital of Anhui Medical University between January 2016 to March 2018 and 102 concurrent female health controls who underwent physical examinations (control group). Serum samples from both groups were subjected to quantitative reverse transcription polymerase chain reaction to measure miR-34a expression. The correlation of miR-34a with BC patients' clinical parameters was analyzed, and the implications of miR-34a for diagnosing BC and predicting NACT efficacy were assessed by receiver operating characteristic curves. Logistic regression analysis was employed to determine whether miR-34a independently influenced treatment effectiveness and patient outcomes. Results: The data showed significantly lower miR-34a levels in the research group than in the control group ($P<0.05$). The area under the curve (AUC) of miR-34a for differentiating BC was 0.888. In BC patients, miR-34a was strongly correlated with tumor staging and differentiation degree. Following NACT, BC patients showed an evident rise in miR-34a expression, with higher levels in patients with effective treatment compared to those with treatment failure ($P<0.05$). The AUC values of serum miR-34a in predicting the efficacy of neoadjuvant chemotherapy from FD to SD and from SD to TD were 0.880 and 0.861, respectively ($P<0.001$). Furthermore, patients with favorable prognosis exhibited markedly higher serum miR-34a expression than those with poor prognosis ($P<0.05$). The AUC of miR-34a expression for predicting adverse prognosis was 0.825. Decreased miR-34a was identified as an independent risk factor for treatment failure and poor prognosis. Conclusions: Taken together, serum miR-34a is downregulated in BC and can predict the clinical progression of BC patients and the therapeutic efficacy of NACT.

Keywords: Breast cancer, serum miR-34a, neoadjuvant chemotherapy, efficacy

Introduction

Breast cancer (BC), the most prevalent malignancy among women, has shown a rising incidence in recent years, with approximately 20 percent of patients progressing to locally advanced disease at the initial presentation [1, 2]. Despite significant advancements in modern molecular diagnostic techniques leading to improved detection and treatment of early BC, managing refractory cases and reducing recurrence rates remain challenging [3, 4].

Preoperative neoadjuvant chemotherapy (NACT) has become a commonly used clinical treatment [5] for BC in recent years. It effectively reduces tumor size, eliminates micrometastases, and increases the chance of breast preservation [6, 7]. While postoperative pathological examination is the gold standard for evaluating treatment efficacy clinically, it has a certain lag [8]. Predicting the NACT efficacy preoperatively and screening BC patients for better outcomes hold crucial significance for patients opting for NACT [9]. MicroRNAs (miRNAs), which selectively bind to the 3'UTR of specific target genes via base complementary pairing, are shown to be strongly associated with the occurrence and development of tumors [10]. In recent years, miRNAs have emerged as potential biomarkers for tumor diagnosis and efficacy prediction [11]. Among them, miR-34a

https://doi.org/10.62347/PHYS4309

has previously been studied as a tumor suppressor that is downregulated in BC tissues [12]. However, few studies have discussed the correlation of miR-34a expression and BC patients' clinicopathological characteristics, as well as its value in predicting the efficacy of NACT.

Accordingly, this study analyzed miR-34a expression in BC patients and its clinical implications for the treatment and efficacy prediction of BC.

Methods and materials

Clinical data

A retrospective analysis was performed on the clinical data of 102 female BC patients (research group) admitted from January 2016 to March 2018 as well as 102 concurrent female health checkups (control group) from The Second Affiliated Hospital of Anhui Medical University. Inclusion criteria were: (1) diagnosis of BC by needle biopsy with surgical indications; (2) acceptance of the NACT scheme; (3) complete clinical and pathological data; (4) provision of preoperative peripheral anticoagulant blood samples. Exclusion criteria included: (1) prior chemoradiotherapy or other anti-tumor treatment before enrollment; (2) pregnancy or lactation; (3) history of other malignant tumors; (4) presence of serious infectious diseases. The Second Affiliated Hospital of Anhui Medical University's Ethics Committee approved the research, which was conducted in compliance with the *Declaration of Helsinki*.

Chemotherapy regimen

All patients received 4 to 6 cycles of preoperative NACT, with 21 days as a chemotherapy cycle. The TEC regimen (docetaxel + epirubicin + cyclophosphamide) was used as follows: On the first day of chemotherapy, patients received 75 mg/m^2 of docetaxel (Jiangsu Aosaikang Pharmaceutical Co., Ltd., SFDA Approval No. H20103653), 75 mg/m^2 of epirubicin (Pharmacia Limited, SFDA Approval No. X20000497), and 500 mg/m^2 of cyclophosphamide (Jiangsu Hengrui Pharmaceuticals, SFDA Approval No. H32026196). Additionally, 7.5 mg of dexamethasone (Xi'an Guokang Ruijin Pharmaceutical Co., Ltd., SFDA Approval No. H20053754) was administered orally twice a day from the day before chemotherapy to the second day of chemotherapy.

Venous blood (6 mL) was drawn from each participant for testing at three different times: before the initiation of chemotherapy (the first detection, FD), at the end of the second cycle (the second detection, SD), and at the end of chemotherapy (the third detection, TD). After discharge, all patients were followed up once a month for 3 years through the WeChat platform, outpatient follow-ups, and home visits. The follow-up was terminated if the patient died within 3 years.

Detection of miR-34a by quantitative reverse transcription polymerase chain reaction (qRT-PCR)

Venous blood was drawn from patients on an empty stomach before and after surgery and centrifuged at a speed of 1500× g for 10 minutes at a temperature of 4°C for serum collection. A total of 3 mL of serum was used, from which total RNA was isolated using Trizol reagent (ThermoFisher, China). The RNA purity and concentration were determined by a NanoDrop ND-1000 spectrophotometer (NanoDrop Technologies, Wilmington, DE, USA). For reverse transcription, 5 μg of the total RNA was converted to cDNA as instructed by the reverse transcription kit (Beijing TransGen Biotech, China). The PCR reaction conditions were 40 cycles of pre-denaturation at 95°C for 60 s, denaturation at 94°C for 10 s, and annealing at 60°C for 45 s. Each sample was tested in triplicate, with 3 duplicate wells per sample. The expression of miR-34a was normalized against U6 and analyzed using $2^{-\Delta\Delta ct}$ method. The primer sequences used for the PCR are provided in **Table 1**.

Outcome measures

(1) The expression of miR-34a in the two groups was observed and its diagnostic value for BC was evaluated; (2) The correlation of miR-34a with BC patients' pathological features was analyzed; (3) The association of miR-34a with NACT efficacy and its predictive value for NACT were determined; (4) The predictive implications of miR-34a for patients' prognoses were discussed; (5) Whether elevated miR-34a was an independent risk factor for poor prognosis

Table 1. Primer sequences

Factors	Upstream primer 5'-3'	Downstream primer 5'-3'
miR-34a	ACACTCCAGCTGGGTGGCAGTGTCTTAGCTGGT	CTCAACTGGTGTCGTGGA
U6	CTCGCTTCGGCAGCACA	AACGCTTCACGAATTTGCGT

Table 2. Comparison of general data

Factors	Research group n=102	Control group n=102	χ^2	P
Age (years old)			0.020	0.887
≥55	61 (59.80)	60 (58.82)		
<55	41 (40.20)	42 (41.18)		
Body mass index (kg/m^2)			0.020	0.887
≥23	58 (56.86)	59 (57.80)		
<23	44 (43.14)	43 (42.16)		
Drinking			0.192	0.661
Yes	67 (65.69)	64 (62.75)		
No	35 (34.31)	38 (37.25)		
Menstrual status			0.019	0.888
Premenopausal	55 (53.92)	54 (52.94)		
Postmenopausal	47 (46.08)	48 (47.06)		
Differentiation degree			-	-
High	21 (20.59)	-		
Moderate	31 (30.39)	-		
Low	50 (49.02)	-		
Pathological staging			-	-
I-II	59 (57.84)	-		
III	43 (42.16)	-		
Pathological classification			-	-
Infiltrating lobular carcinoma	71 (69.61)	-		
Invasive ductal carcinoma	31 (30.39)	-		

was identified by the logistic regression analysis.

Statistical methods

The collected experimental data were imported into SPSS19.0 for statistical analysis. Chi-square tests were used for count data, while independent t-tests were for measurement data statistically described as the mean ± standard deviation. Graphs depicting the experiment results were generated using GraphPad Prism 6. The value of miR-34a in diagnosing BC was assessed by receiver operating characteristic (ROC) curves, and the risk factors for adverse prognosis in BC patients were identified by the logistic regression model. Statistical significance was defined as P<0.05.

Results

Comparison of general information

The two groups were clinically comparable, with no significant inter-group difference in gender, age, body mass index, and other baseline data (P>0.05), as shown in **Table 2**.

Expression and diagnostic implications of miR-34a for BC

The serum levels of miR-34a is lower in research group than in control group (P<0.05). miR-34a had an area under the curve (AUC) of 0.888 in diagnosing BC, suggesting high diagnostic value of miR-34a. See **Figure 1**.

Correlation of miR-34a with BC patients' pathological features

miR-34a levels altered little in BC cases of different ages, pathological types, and tumor sizes (P>0.05); however, miR-34a showed a significant association with tumor differentiation and pathological staging (P<0.05). Refer to **Table 3** for details.

Association of miR-34a with NACT efficacy

Following NACT, among the 102 patients, 33 achieved complete remission, 37 had partial remission, 28 had a stable disease, and 4 developed a progressive disease. Therefore, 70 cases were included in the effective group, while 32 were in the ineffective group. Peripheral blood miR-34a levels at FD, SD, and TD were significantly reduced in patients with ineffective treatment compared to those with effective treatment at the corresponding time point (P<0.05). See **Figure 2**.

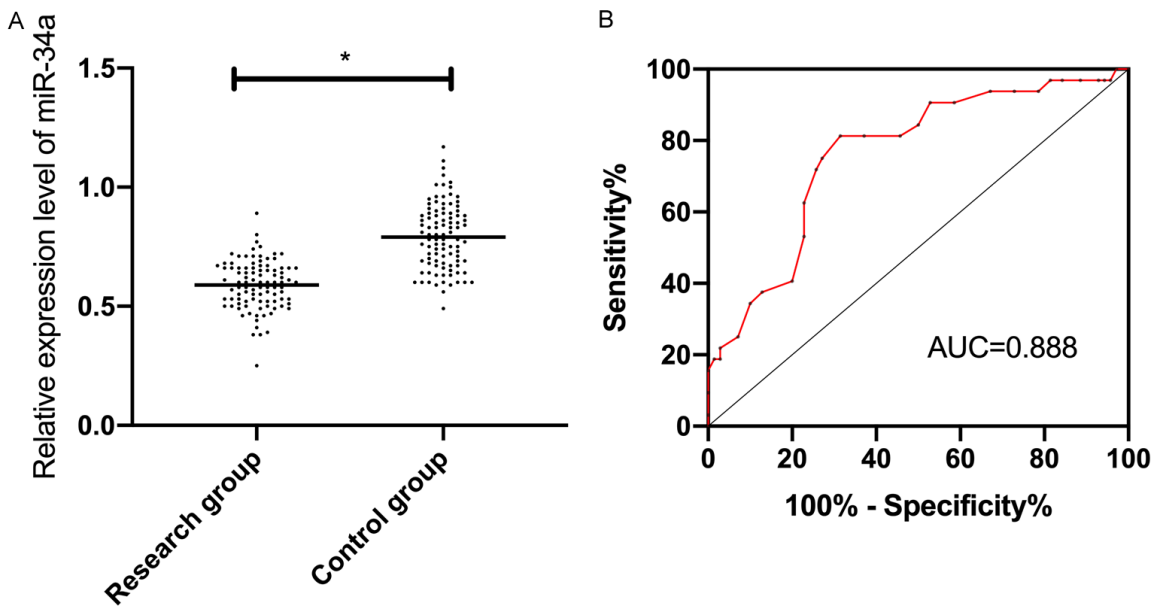

Figure 1. miR-34a expression and its diagnostic value in breast carcinoma; A: miR-34a levels in breast carcinoma patients; B: ROC curve of miR-34a in diagnosing breast carcinoma (AUC=0.888). *P<0.05. ROC, receiver operating characteristic.

Table 3. Correlation of miR-34a expression with patients' clinicopathological features

Factors	Relative miR-34a expression	t/F value	*P* value
Age		1.826	0.071
≥55 (n=61)	0.43±0.05		
<55 (n=41)	0.45±0.06		
TNM stage		11.57	<0.001
I-II (n=59)	0.57±0.07		
III (n=33)	0.41±0.05		
Tumor size		1.624	0.108
≥5 cm (n=42)	0.46±0.06		
<5 cm (n=60)	0.44±0.05		
Pathological type		3.223	0.002
Infiltrating lobular carcinoma (n=71)	0.42±0.04		
Invasive ductal carcinoma (n=31)	0.45±0.05		
Differentiation degree		0.969	0.031
High (n=21)	0.57±0.08		
Moderate (n=31)	0.49±0.06		
Low (n=50)	0.37±0.04		

Predictive value of miR-34a for the efficacy of NACT

The AUCs of serum miR-34a in predicting the efficacy of NACT from FD to SD and from SD to TD were 0.880 and 0.861, respectively (P<0.001). See **Figure 3**.

Prognostic value of miR-34a in BC

Depending on patient prognosis, 75 cases were assigned to the survival group and 27 cases to the death group. The intergroup comparison of serum miR-34a expression showed statistically higher miR-34a levels in the survival group than the death group (P<0.05). Moreover, ROC analysis revealed that miR-34a had a high predictive value for poor prognosis of BC patients, with an AUC of 0.825. See **Figure 4**.

miR-34a is an independent factor influencing patient efficacy and prognosis

The occurrence of treatment failure or poor prognosis was set as the dependent variable (treatment failure or poor prognosis was assigned a value of 1), and changes in miR-34a (elevation =1, non-elevation =0) were considered as the independent variable. Decreased miR-34a was confirmed as an independent risk factor for treatment failure and poor prognosis (P<0.05). Refer to **Table 4** for details.

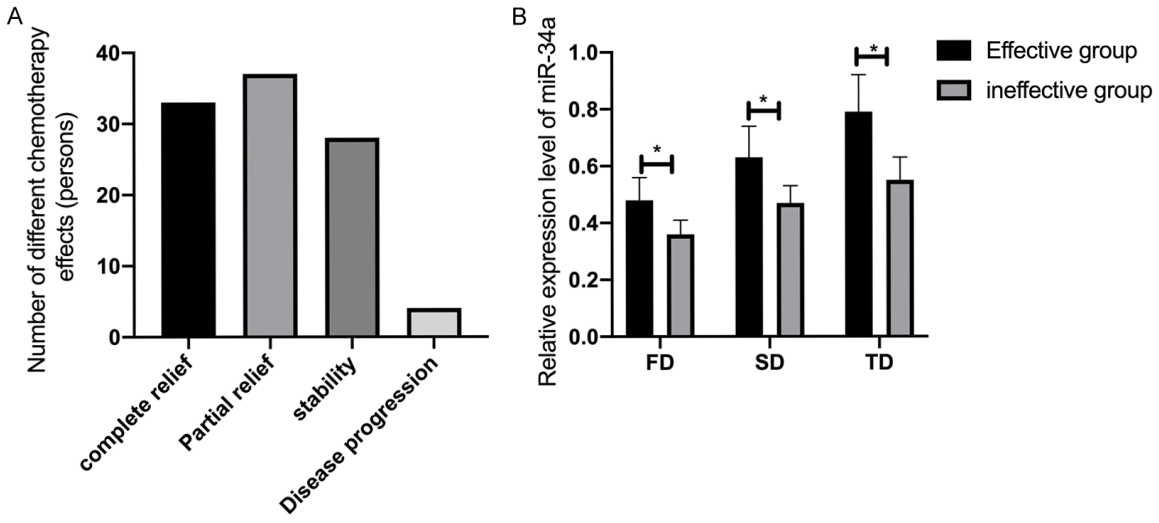

Figure 2. Association of miR-34a with neoadjuvant chemotherapy efficacy; A: Chemotherapy efficacy in breast carcinoma patients; B: miR-34a expression in patients with different therapeutic effects at different time points. *P<0.05.

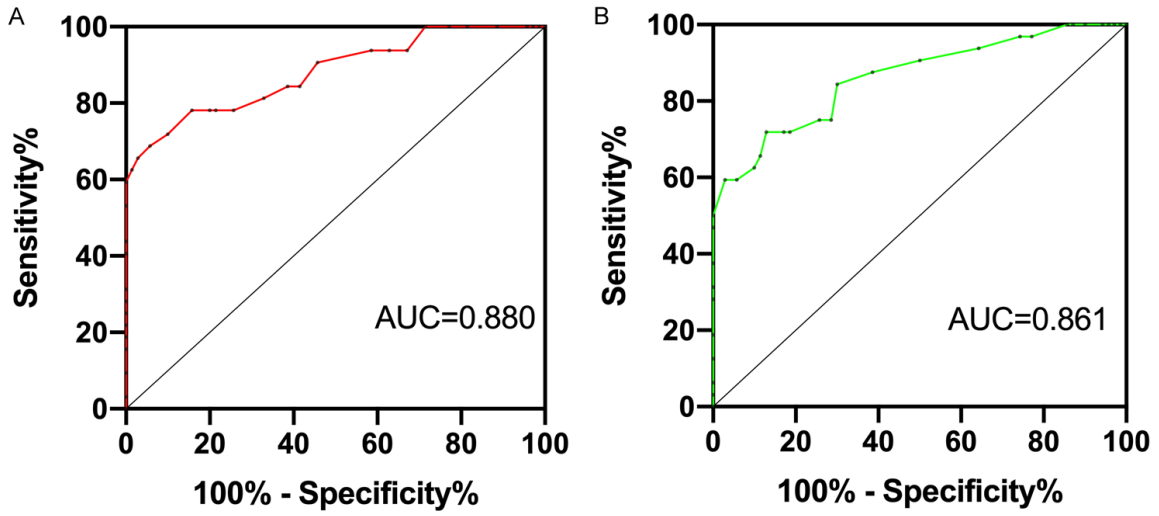

Figure 3. Predictive value of miR-34a for the efficacy of neoadjuvant chemotherapy; A: The AUC of miR-34a for predicting the efficacy from FD to SD was 0.880 (P<0.001); B: The AUC of miR-34a in predicting the efficacy from SD to TD was 0.861 (P<0.001). FD, the first detection; SD, the second detection; TD, the third detection.

Discussion

BC is one of the most common malignancies in women. Despite considerable progress made in BC diagnosis and management with the advancement in medical technology, the disease and chemoradiotherapy-induced adverse effects continue to severely impact patients' quality of life [13, 14]. Multiple miRNAs have now been indicated to be essential in BC diagnosis and treatment as molecular biology advances [15].

Previous studies have revealed significant differences in miR-34a expression in different tumors. In this study, serum miR-34a levels were quantified by PCR, revealing a statistically significant reduction in BC cases compared to controls. However, there are still conflicting findings regarding whether miR-34a acts as a carcinogenic or anticancer agent. As reported by Yang et al. [16], miR-34a was statistically reduced in both BC cells and tissues with lymph node metastasis, and overexpression of miR-34a could inhibit BC invasion and metastasis.

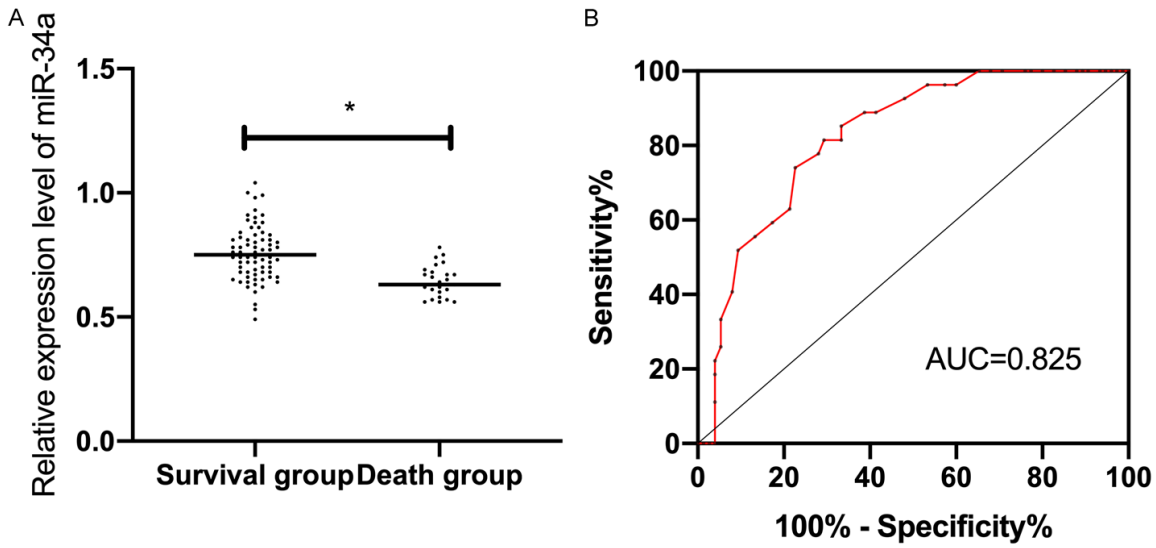

Figure 4. Prognostic value of miR-34a for breast carcinoma; A: Serum miR-34a levels in patients with different prognoses; B: ROC analysis of miR-34a in predicting patients' prognoses (AUC=0.825). *P<0.05. ROC, receiver operating characteristic.

Table 4. miR-34a is an independent factor affecting treatment efficacy and patient prognosis

Dependent variable	B	S.E.	Wals	P	OR	95% C.I.	
						Lower bound	Upper bound
Treatment failure	1.114	0.581	4.629	0.019	3.293	1.155	10.238
Poor prognosis	1.479	0.623	5.201	0.022	4.435	1.296	14.825

Another study [17] suggests that miR-34a functions as a tumor suppressor in prostate cancer. There is also research indicating that miR-34a can inhibit BC cell proliferation and invasion [18], consistent with our findings. However, some studies have reached opposite conclusions. For example, a study [19] showed that miR-34a is highly expressed in BC tissue by in situ hybridization. These conflicting results indicate that the role of miR-34a in many cancers, including BC, is complex and requires further in-depth investigation.

Today, miRNAs show great potential in the diagnosis, prognosis assessment, and prediction of chemotherapy efficacy for cancers and other diseases. They can be stably expressed in blood, offering advantages such as non-invasiveness, the ability for repeated sampling, and dynamic monitoring of disease progression [20]. Our study further analyzed the implications of miR-34a for diagnosing BC by ROC, revealing its high diagnostic value and suggesting its potential significance in BC diagnosis. To better understand the association of miR-34a with BC, we examined the relationship between miR-34a and BC patients' clinicopathological features and found a close connection between miR-34a and tumor differentiation and pathological staging. Similar conclusions were drawn in previous research. For example, Hagrass et al. [21] confirmed markedly reduced serum miR-34a in BC patients compared to healthy individuals, with even lower miR-34a levels in stage M1 patients than in stage M0 patients. This suggests that altered miR-34a expression may be an independent evaluation target and an independent risk factor for BC, but further analysis is required.

Multiple miRNAs are associated with NACT efficacy in BC. For instance, in BC patients receiving NACT with epirubicin plus docetaxel, serum miR-451 expression levels before the start of chemotherapy were statistically lower in chemotherapy-resistant group than in chemotherapy-sensitive group [22], demonstrating that pre-chemotherapy serum miR-451 levels can

predict the sensitivity of NACT. Another study [23] reveals that miRNA-621 sensitizes BC to chemotherapy via suppressing FBXO11 and enhancing p53 activity. Additionally, miR-34a has a close relationship with chemotherapy resistance in many BC tissue and cell studies. One study [24] analyzed miR-34a expression in BC and found that it was closely related to the sensitivity of NACT. However, whether miR-34a expression can serve as a predictive marker for BC chemotherapy has not been reported. In our study, we detected gradually elevated miR-34a in BC patients as chemotherapy progressed, particularly in those with effective treatment. Subsequently, we analyzed the predictive value of miR-34a for curative effects. ROC curve analysis revealed that serum miR-34a expression in patients after two cycles of chemotherapy had an accuracy of 0.880 in predicting chemotherapy efficacy, suggesting that the dynamic change of serum miR-34a can serve as a biomarker to predict the efficacy of NACT in BC. Moreover, the dynamic alterations in serum miR-34a levels reflect changes in the disease course, making it useful for monitoring after NACT and surgery, which will assist in the early detection of BC recurrence. Also, we analyzed the correlation of miR-34a with BC patients' prognoses and found statistically higher serum miR-34a in patients with favorable prognosis. In BC patients post-chemotherapy, miR-34a had a high predictive value for poor prognosis. Previous research [25] has also affirmed the role of miRNAs in predicting treatment effectiveness and outcomes of BC patients, noting that miRNAs can be used as complementary tools for BC diagnosis, prognosis assessment, and efficacy prediction due to their simplicity of detection and reproducibility in laboratory tests.

In conclusion, miR-34a is lowly-expressed in BC, with high value in diagnosing BC, predicting NACT efficacy, and assessing patient prognosis. It is of great clinical significance for formulating individualized treatment plans for BC patients, adjusting post-NACT treatment protocols, avoiding unnecessary overtreatment, and improving treatment effectiveness. However, this study still shows some limitations. Firstly, the findings need to be validated by further large-sample multi-center studies. Additionally, since this study only analyzed a single indicator of miR-34a, further exploration is warranted to ascertain whether its combined use with other common indicators can further enhance its clinical application value.

Acknowledgements

This study was supported by 2023 Anhui Provincial Clinical Medical Research Transformation Special Project "Phase II clinical study of neoadjuvant endocrine combined with chemotherapy in the treatment of ER-positive HER2-negative stage I-III breast cancer" (202304295107020024).

Disclosure of conflict of interest

None.

Address correspondence to: Zhendong Chen, Department of Oncology, The Second Affiliated Hospital of Anhui Medical University, Hefei 230601, Anhui, China. Tel: +86-0551-63869536; E-mail: chenzhendong_hefei@163.com

References

[1] Zhao W, Geng D, Li S, Chen Z and Sun M. LncRNA HOTAIR influences cell growth, migration, invasion, and apoptosis via the miR-20a-5p/HMGA2 axis in breast cancer. Cancer Med 2018; 7: 842-855.

[2] Mansoori B, Najafi S, Mohammadi A, AsadollahSeraj H, Savadi P, Mansoori B, Nazari A, Mokhtarzadeh A, Roshani E, Duijf PH, Cho WC and Baradaran B. The synergy between miR-486-5p and tamoxifen causes profound cell death of tamoxifen-resistant breast cancer cells. Biomed Pharmacother 2021; 141: 111925.

[3] Kheradmand P, Vallian Boroojeni S and Esmaeili-Mahani S. MiR-221 expression level correlates with insulin-induced doxorubicin resistance in MCF-7 breast cancer cells. Cell J 2021; 23: 329-334.

[4] Liu H and Wang G. MicroRNA-301a-3p promotes triple-negative breast cancer progression through downregulating MEOX2. Exp Ther Med 2021; 22: 945.

[5] Cao S, Liu X, Cui J, Liu X, Zhong J, Yang Z, Sun D and Wei W. Feasibility and reliability of sentinel lymph node biopsy after neoadjuvant chemotherapy in breast cancer patients with positive axillary nodes at initial diagnosis: an up-to-date meta-analysis of 3,578 patients. Breast 2021; 59: 256-269.

[6] Wu W, Chen J, Deng H, Jin L, He Z, Rao N, Nie Y, Yao Y, Yang Y, Su F and Liu J. Neoadjuvant everolimus plus letrozole versus fluorouracil,

epirubicin and cyclophosphamide for ER-positive, HER2-negative breast cancer: a randomized pilot trial. BMC Cancer 2021; 21: 862.
[7] Gil-Gil MJ, Bellet M, Bergamino M, Morales S, Barnadas A, Manso L, Saura C, Fernandez-Ortega A, Garcia-Martinez E, Martinez-Janez N, Mele M, Villagrasa P, Celiz P, Perez Martin X, Ciruelos E and Pernas S. Long-term cardiac safety and survival outcomes of neoadjuvant pegylated liposomal doxorubicin in elderly patients or prone to cardiotoxicity and triple negative breast cancer. Final results of the multicentre phase II CAPRICE study. Front Oncol 2021; 11: 645026.
[8] Verdial FC, Mamtani A, Pawloski KR, Sevilimedu V, D'Alfonso TM, Zhang H, Gemignani ML, Barrio AV, Morrow M and Tadros AB. The effect of age on outcomes after neoadjuvant chemotherapy for breast cancer. Ann Surg Oncol 2022; 29: 3810-3819.
[9] Ogino M, Fujii T, Koibuchi Y, Nakazawa Y, Takata D and Shirabe K. Phase II study of nab-paclitaxel plus cyclophosphamide plus trastuzumab neoadjuvant chemotherapy in early HER-2-positive breast cancer. Anticancer Res 2021; 41: 3899-3904.
[10] Wang X, Zhou X, Zeng F, Wu X and Li H. miR-485-5p inhibits the progression of breast cancer cells by negatively regulating MUC1. Breast Cancer 2020; 27: 765-775.
[11] Zhang H, Zheng XD, Zeng XH, Li L and Zhou Q. miR-520b inhibits IGF-1R to increase doxorubicin sensitivity and promote cell apoptosis in breast cancer. Yakugaku Zasshi 2021; 141: 415-426.
[12] Shi SH, Jiang J, Zhang W, Sun L, Li XJ, Li C, Ge QD and Zhuang ZG. A novel lncRNA HOXC-AS3 acts as a miR-3922-5p sponge to promote breast cancer metastasis. Cancer Invest 2020; 38: 1-12.
[13] Zhao L, Han S, Hou J, Shi W, Zhao Y and Chen Y. The local anesthetic ropivacaine suppresses progression of breast cancer by regulating miR-27b-3p/YAP axis. Aging (Albany NY) 2021; 13: 16341-16352.
[14] Lei B, Wang D, Zhang M, Deng Y, Jiang H and Li Y. miR-615-3p promotes the epithelial-mesenchymal transition and metastasis of breast cancer by targeting PICK1/TGFBRI axis. J Exp Clin Cancer Res 2020; 39: 71.
[15] Shen Y, Xu Y, Huang L, Chi Y and Meng L. MiR-205 suppressed the malignant behaviors of breast cancer cells by targeting CLDN11 via modulation of the epithelial-to-mesenchymal transition. Aging (Albany NY) 2021; 13: 13073-13086.
[16] Yang S, Li Y, Gao J, Zhang T, Li S, Luo A, Chen H, Ding F, Wang X and Liu Z. MicroRNA-34 suppresses breast cancer invasion and metastasis by directly targeting Fra-1. Oncogene 2013; 32: 4294-4303.
[17] Yan X, Tang B, Chen B, Shan Y and Yang H; Reproducibility Project: Cancer Biology. Replication study: the microRNA miR-34a inhibits prostate cancer stem cells and metastasis by directly repressing CD44. Elife 2019; 8: e43511.
[18] Han R, Zhao J and Lu L. MicroRNA-34a expression affects breast cancer invasion in vitro and patient survival via downregulation of E2F1 and E2F3 expression. Oncol Rep 2020; 43: 2062-2072.
[19] Dutta KK, Zhong Y, Liu YT, Yamada T, Akatsuka S, Hu Q, Yoshihara M, Ohara H, Takehashi M, Shinohara T, Masutani H, Onuki J and Toyokuni S. Association of microRNA-34a overexpression with proliferation is cell type-dependent. Cancer Sci 2007; 98: 1845-1852.
[20] Anwar SL, Tanjung DS, Fitria MS, Kartika AI, Sari DNI, Rakhmina D, Wardana T, Astuti I, Haryana SM and Aryandono T. Dynamic changes of circulating mir-155 expression and the potential application as a non-invasive biomarker in breast cancer. Asian Pac J Cancer Prev 2020; 21: 491-497.
[21] Hagrass HA, Sharaf S, Pasha HF, Tantawy EA, Mohamed RH and Kassem R. Circulating microRNAs - a new horizon in molecular diagnosis of breast cancer. Genes Cancer 2015; 6: 281-287.
[22] Gu X, Xue JQ, Han SJ, Qian SY and Zhang WH. Circulating microRNA-451 as a predictor of resistance to neoadjuvant chemotherapy in breast cancer. Cancer Biomark 2016; 16: 395-403.
[23] Xue J, Chi Y, Chen Y, Huang S, Ye X, Niu J, Wang W, Pfeffer LM, Shao ZM, Wu ZH and Wu J. MiRNA-621 sensitizes breast cancer to chemotherapy by suppressing FBXO11 and enhancing p53 activity. Oncogene 2016; 35: 448-458.
[24] Freres P, Josse C, Bovy N, Boukerroucha M, Struman I, Bours V and Jerusalem G. Neoadjuvant chemotherapy in breast cancer patients induces miR-34a and miR-122 expression. J Cell Physiol 2015; 230: 473-481.
[25] Jordan-Alejandre E, Campos-Parra AD, Castro-Lopez DL and Silva-Cazares MB. Potential miRNA use as a biomarker: from breast cancer diagnosis to metastasis. Cells 2023; 12: 525.