Pharmacogenomics and Personalized Medicine

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Construction of a Nomogram Model for Predicting Prognosis in Breast Cancer Patients Based on the Expression of THRSP and ACACA Proteins Tissues

Benkai Wei*, Fan Li*, Huanhuan Yan, Jun Shen

Department of Breast Surgery, The First People's Hospital of Lianyungang, Lianyungang, Jiangsu, 222002, People's Republic of China

*These authors contributed equally to this work

Correspondence: Jun Shen, Department of Breast Surgery, The First People's Hospital of Lianyungang, No. 6 Zhenhua East Road, High-Tech Square, Lianyungang, Jiangsu, 222002, People's Republic of China, Email ShenJunsj2004@126.com

Background: This study aimed to analyze the expression of thyroid hormone-responsive spot 14 (THRSP) and acetyl-CoA carboxylase alpha (ACACA) proteins in breast cancer tumor tissues and their relationship with clinicopathology and prognosis of breast cancer patients. In addition, a nomogram model to predict the prognosis of breast cancer patients was constructed in this study.

Methods: Retrospective analysis of 202 cases of breast cancer patients who underwent surgical treatment in our hospital from October 2019 to March 2021, and collection of patients' cancer tissues and non-Tumor tissue specimens. Immunohistochemistry was used to detect THRSP and ACACA protein expression. Multivariate COX regression was used to analyze the risk factors affecting the prognosis of breast cancer patients. The "rms" package in R software was used to build a survival nomogram model and evaluate the effectiveness of the model.

Results: The expression of THRSP and ACACA proteins in tumor tissues of breast cancer patients was higher than that in non-tumor tissues ($p < 0.05$). The expression of THRSP and ACACA proteins in breast cancer patients with lymph node metastasis was higher than that in patients without lymph node metastasis ($p < 0.05$). Cox regression analysis showed that TNM stage III, lymph node metastasis, high expression of Ki-67, high expression of THRSP, and high expression of ACACA were all risk factors for the prognosis of breast cancer patients ($p < 0.05$). The C-index of the nomogram model was 0.704 (95% CI: 0.596~0.892). The predicted 1-, 2- and 3-year survival AUCs of this nomogram model were 0.802, 0.769 and 0.770, respectively. The calibration curve showed that the model fit the ideal curve well. Decision curve analysis showed the high clinical utility of the model.

Conclusion: The nomogram model constructed based on THRSP and ACACA proteins may provide a reference value for the prognostic evaluation of breast cancer patients.

Keywords: thyroid hormone responsive spot 14, acetyl-CoA carboxylase α, breast cancer, prognosis

Introduction

Breast cancer is a global issue, with an increasing incidence year by year, and its high mortality rate poses a serious threat to women's health and lives.[1] In addition, breast cancer accounts for 30% of all female cancers and 15–20% of all female cancer deaths.[2] In recent years, with the improvement of diagnosis and treatment, the mortality rate of breast cancer has been reduced. However, there is a problem of delayed diagnosis in less developed areas, and more than half of breast cancer patients are in locally advanced or metastatic stages at the time of diagnosis. In addition, because breast cancer is highly heterogeneous at the morphological and molecular levels, its etiology and pathologic manifestations vary from person to person, and patients are prone to poor prognosis such as recurrence or treatment resistance.[3] Therefore, it is of great significance to accurately assess the prognosis of breast cancer patients and improve patient survival rate and quality of life.

Received: 10 January 2025
Accepted: 7 May 2025
Published: 31 July 2025

Thyroid hormone responsive spot 14 (THRSP) is mainly involved in fatty acid synthesis and metabolism.[4] Recent studies have found that THRSP is strongly expressed in most adipose breast cancers, and high expression of THRSP predicts a high recurrence rate of primary invasive breast cancer, suggesting that there may be a relationship between THRSP protein expression and pathophysiological mechanisms of breast cancer.[5] Acetyl-CoA carboxylase α (ACACA) is a key enzyme in the fatty acid synthesis pathway. Bacci et al[6] found that ACACA-1 promotes lipid mobilization in estrogen-deprived breast cancer cells, leading to resistance to estrogen therapy, and hypothesized that ACACA may be related to the treatment outcome of breast cancer and affect patient prognosis. The current nomogram model for the prognosis of breast cancer relies mostly on traditional clinical and pathological factors, such as tumor size, lymph node metastasis status, pathological stage, and molecular markers such as estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2).[7,8] There are few literature reports on prediction models based on THRSP and ACACA proteins. In view of this, this study will build a nomogram model for the prognosis of breast cancer patients based on the expression of THRSP and ACACA proteins in tumor tissue, in order to make up for the shortcomings of existing prediction models.

Materials and Methods

Patients

Two hundred and two breast cancer patients admitted to our hospital from January 2019 to March 2021 were selected as study subjects. Inclusion criteria: (1) all were female; (2) diagnosed with breast cancer by clinicopathologic examination[9] and admitted to the hospital to receive surgical treatment; (3) all were older than 18 years old; (4) TNM staging[10] was stage I to III. Exclusion criteria: (1) those with other malignant tumors; (2) those with acute and chronic infections and immune system diseases; (3) those who were in pregnancy and lactation; (4) those with mental disorders; and (5) those with cardiac, hepatic, and renal vital organ insufficiency. This study was approved by the Hospital Ethics Committee of the First People's Hospital of Lianyungang.

Data Collection

Clinical data of all breast cancer patients were collected, including age, tumor diameter, tumor site, TNM stage, lymph node metastasis, and Ki-67 expression. A hollow core needle was used to puncture the biopsy tissue, and Ki-67 protein expression was detected by immunohistochemistry. The presence of brownish-yellow granules in the nucleus was regarded as positive, and the proportion of positive cells ≥15% was regarded as high expression, and vice versa was regarded as low expression.

Immunohistochemistry

Paraffin sections (4 μm) were baked, deparaffinized, and hydrated, and then antigenically repaired with citric acid antigen repair solution (pH=6.0) for 2 min. After rinsing with phosphate buffer solution (PBS), the sections were incubated with 3% hydrogen peroxide for 10 min at room temperature. After rinsing in PBS, rabbit anti-human THRSP polyclonal antibody (1:500 dilution, Beyotime, Shanghai, China) and mouse anti-human ACACA polyclonal antibody (1:2000 dilution, Beyotime, Shanghai, China) were added dropwise to the sections and incubated for 1 h at room temperature. Ready-to-use MaxVision detection reagent was added dropwise to the sections and incubated at room temperature for 15 min. After DAB color development, the sections were stained with hematoxylin. After rinsing with PBS to return the blue color and dehydration with gradient ethanol, the sections were fixed with xylene clear and neutral gum sealer. The results were determined by two experienced pathologists, and positive cells were recognized by the presence of yellowish, tan or brownish staining in the nucleus or cytoplasm. The results were scored according to the intensity of staining and the percentage of positive cells: (1) Scoring of the percentage of positive cells: less than 5% is 0 points, 5–25% is 1 point, 25–50% is 2 points, 50–75% is 3 points, and 75% or more is 4 points; (2) Staining intensity: 0 points for no staining, 1 point for yellow or light yellow, 2 points for tan, and 3 points for brown. Staining index (SI) = proportion of positive cells×staining intensity, SI > 3 points was recorded as high expression, SI ≦ 3 was recorded as low expression.

Follow-Up

The patients were followed up (by telephone or outpatient clinic) as soon as they were discharged from the hospital, every month in the first year, every 3 months in the second year, and every 6 months thereafter, and the follow-up was terminated if the patient died. The follow-up cut-off date was January 2024, with a total of 52 months of follow-up and a median follow-up time of 48 months. Overall survival (OS) was defined as the time from the start of follow-up until the patient's death or the end of follow-up.

Statistical Analyses

SPSS 26.0 software (Chicago, IL, USA) was used to analyze the data of this study statistically. Measurement data of normal distribution were described as mean ± standard deviation, and a *t*-test was used. Count data were expressed as examples and compared using the $\chi 2$ test. A difference of $p < 0.05$ was considered statistically significant. Kaplan-Meier method was used to draw survival curves, and the Log rank test was used for comparison. The Multivariable Cox regression model was used to analyze the influencing factors of prognosis in breast cancer patients. Based on the results of multifactorial Cox regression analysis, the nomogram model was constructed using the "rms" package in R language. The consistency of the nomogram model was evaluated using the consistency index (C-index), and the internal validation of the original data was performed by setting Bootstrap to 1000 times. ROC curves were used to assess the predictive performance of the nomogram model. Plotting calibration curves was used to assess the predictive compliance of the model. Decision curve analysis was used to assess the clinical value of the model. The two-sided test level α was 0.05.

Results

Comparison of THRSP and ACACA Protein in Tumor and Non-Tumor Tissues of Breast Cancer Patients

THRSP and ACACA proteins in breast cancer tissues were localized in the cytoplasm and was yellowish to tan in color (Figure 1). The percentage of high expression of THRSP and ACACA proteins in tumor tissues of breast cancer patients was higher than that in non-tumor tissues ($p < 0.05$, Table 1).

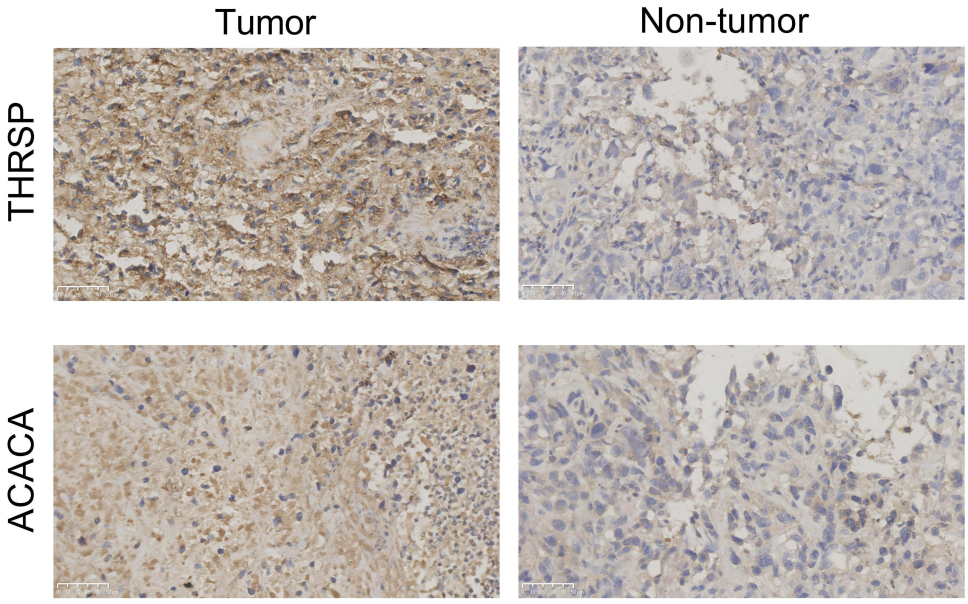

Figure 1 Detection of THRSP and ACACA protein in tumor and non-tumor tissues by immunohistochemical analysis.

https://doi.org/10.2147/PGPM.S516843

Table 1 THRSP and ACACA Protein Expression in Tumor and Non-Tumor Tissues of Breast Cancer Patients

Group	n	THRSP Protein		ACACA Protein	
		High Expression	Low Expression	High Expression	Low Expression
Tumor	202	76	126	97	105
Non-Tumor	202	18	184	37	165
χ^2		10.569		18.687	
p		0.001		<0.001	

Abbreviations: THRSP, hyroid hormone responsive spot 14; ACACA, acetyl-CoA carboxylase α.

Relationship Between THRSP/ACACA and Clinicopathological Characteristics of Breast Cancer Patients

There was no statistically significant difference in the comparison of THRSP, ACACA protein expression in breast cancer patients with different ages, tumor diameters, tumor sites, TNM stages, histological grades, and Ki-67 expression (P > 0.05, Table 2). The percentage of THRSP high expression and ACACA high expression in breast cancer patients with lymph node metastasis was higher than that in patients without lymph node metastasis ($p < 0.05$, Table 2).

Table 2 Relationship Between THRSP/ACACA and Clinicopathologic Characteristics of Breast Cancer Patients

Clinicopathologic Features	n	THRSP Protein			ACACA Protein		
		High Expression	χ^2	*p*	High Expression	χ^2	*p*
Age			0.272	0.602		0.382	0.537
≤50 years old	71	25			32		
>50 years old	131	51			65		
BMI			1.860	0.173		2.638	0.104
≤24 kg/cm^2	86	37			47		
>24 kg/cm^2	116	39			50		
Tumor Diameter			1.562	0.211		1.020	0.313
<2 cm	141	57			71		
≥2 cm	61	19			26		
Tumor Location			2.988	0.084		1.685	0.194
Left side	132	44			59		
Right side	70	32			38		
TNM Stage			1.752	0.186		3.831	0.050
Stage I~II	70	22			27		
Stage III	132	54			70		
Histologic grading			3.649	0.056			
I–II	136	45			60	2.539	0.111
III	66	31			37		
Lymph node metastasis			8.374	0.004		6.650	0.010
No	79	20			29		
Yes	123	56			67		
Ki-67			0.131	0.718		0.043	0.835
Low expression	66	26			31		
Highly expressed	136	50			66		

Abbreviations: BMI, body mass index; THRSP, thyroid hormone responsive spot 14; ACACA, acetyl-CoA carboxylase α.

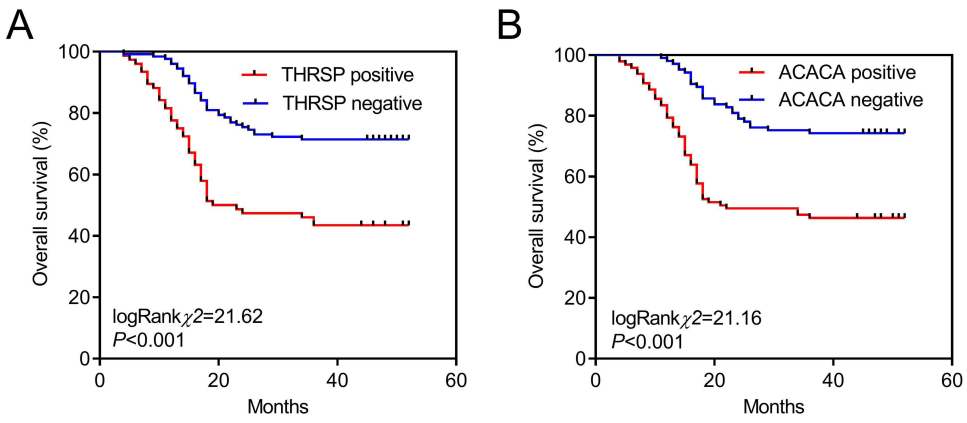

Figure 2 Kaplan-Meier survival curves. (**A**) THRSP protein; (**B**) ACACA protein.

Relationship Between THRSP/ACACA and Prognosis of Breast Cancer Patients

The results of Kaplan-Meier survival curves showed that patients with high expression of THRSP and high expression of ACACA had worse survival than patients with low expression of THRSP and low expression of ACACA (log-rank $\chi2 = 21.62$, $p < 0.001$; log-rank $\chi2 = 21.16$, $p < 0.001$, Figure 2).

Multivariate Cox Regression Analysis Affecting the Prognosis of Breast Cancer Patients

Univariate regression analysis showed that TNM stage, lymph node metastasis, Ki-67, THRSP, and ACACA were associated with the prognosis of breast cancer patients ($p < 0.05$, Table 3). The prognosis of breast cancer patients was taken as the dependent variable, and multifactorial Cox regression analysis was performed with age, tumor diameter, tumor site, TNM stage, lymph node metastasis, Ki-67, THRSP, and ACACA as the independent variables. The results showed that TNM stage III, lymph node metastasis, high expression of Ki-67, high expression of THRSP, and high expression of ACACA were independent risk factors for the prognosis of breast cancer patients ($p < 0.05$, Table 3).

Predictive Modeling and Performance Evaluation

Based on the results of multivariate Cox regression analysis, a nomogram prediction model for predicting the survival rate of breast cancer patients was established with TNM stage III, lymph node metastasis, high Ki-67 expression, high

Table 3 Univariate and Multivariate Cox Regression Analysis of Prognosis in Breast Cancer Patients

	Univariate			Multivariate		
	HR	**95% CI**	***p***	***HR***	**95% CI**	***p***
Age (>50 years)	0.722	0.433–1.202	0.210			
BMI > (24 kg/cm2)	0.824	0.501–1.355	0.445			
Tumor diameter (≥2cm)	1.200	0.692–2.082	0.516			
Tumor site (left side)	1.588	0.981–2.571	0.060			
TNM staging (stage III)	3.663	1.975–6.791	<0.001	3.955	2.169–7.21	<0.001
Histologic grading (grade III)	1.860	1.146–3.017	0.012			
Lymph node metastasis	2.523	1.522–4.183	<0.001	2.593	1.586–4.241	<0.001
Ki-67 high expression	3.323	1.815–6.082	<0.001	3.200	1.817–5.637	<0.001
THRSP high expression	2.033	1.140–3.626	0.016	2.113	1.221–3.659	0.008
ACACA high expression	2.203	1.235–3.932	0.008	2.527	1.407–4.537	0.002

Abbreviations: BMI, body mass index; THRSP, thyroid hormone responsive spot 14; ACACA, acetyl-CoA carboxylase α.

https://doi.org/10.2147/PGPM.S516843

THRSP expression, and high ACACA expression (Figure 3). Further internal validation using Bootstrap resampling method found that the C-index of this nomogram was 0.704 (95% CI: 0.596~0.892), suggesting that the predicted values obtained from the nomogram were in good agreement with the actual observed values. The AUC of the nomogram model for predicting 1-year, 2-year and 3-year survival were 0.802, 0.769 and 0.770 (Figure 4A–C), suggesting that the model had good predictive efficacy. The calibration curve showed that the experimental values fitted well with the standard curve (Figure 5A–C), suggesting that the nomogram model was well-calibrated. Decision curve analysis showed that the predictive model had a high overall net benefit in predicting the prognosis of immunotherapy in NSCLC patients when the threshold probability was 0.2 to 1.0 (Figure 6).

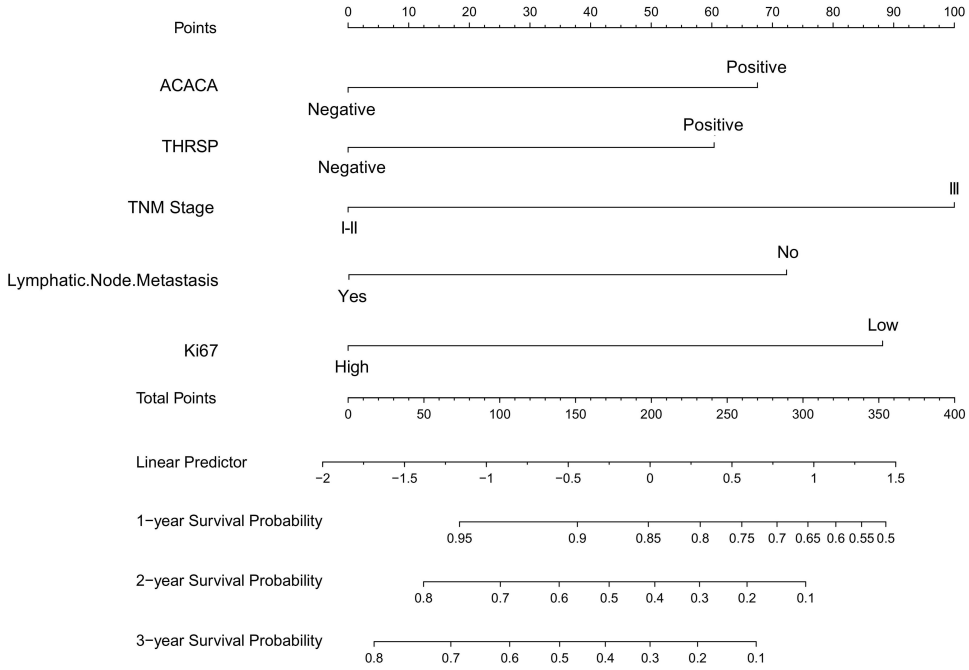

Figure 3 A nomogram model for predicting the prognosis of immunotherapy in NSCLC patients.

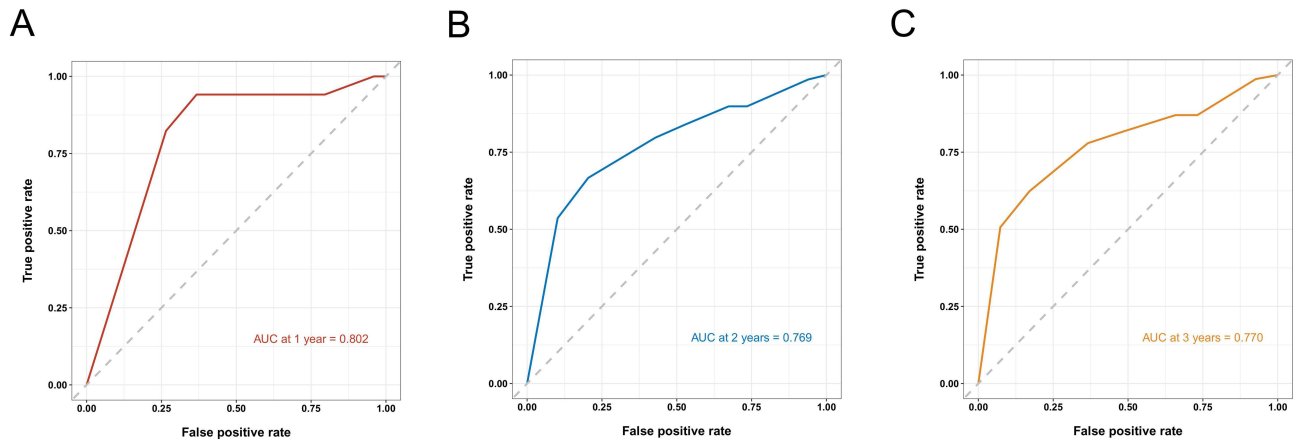

Figure 4 Receiver operating characteristic (ROC) curve of nomogram model. (**A**) 1-year survival rate; (**B**) 2-year survival rate; (**C**) 3-year survival rate.

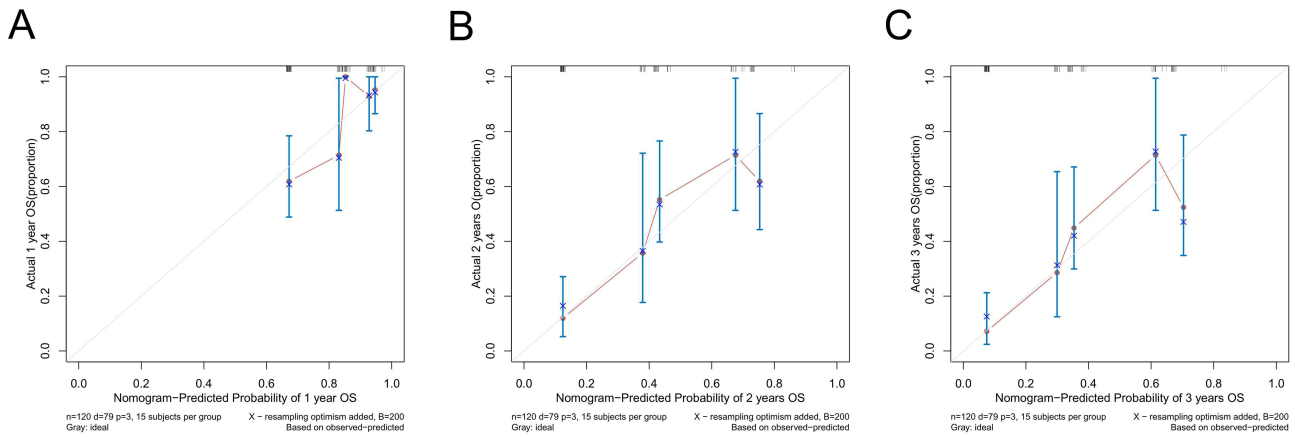

Figure 5 Calibration curves for nomogram models. (**A**) Prediction of 1-year survival; (**B**) Prediction of 2-year survival; (**C**) Prediction of 3-year survival.

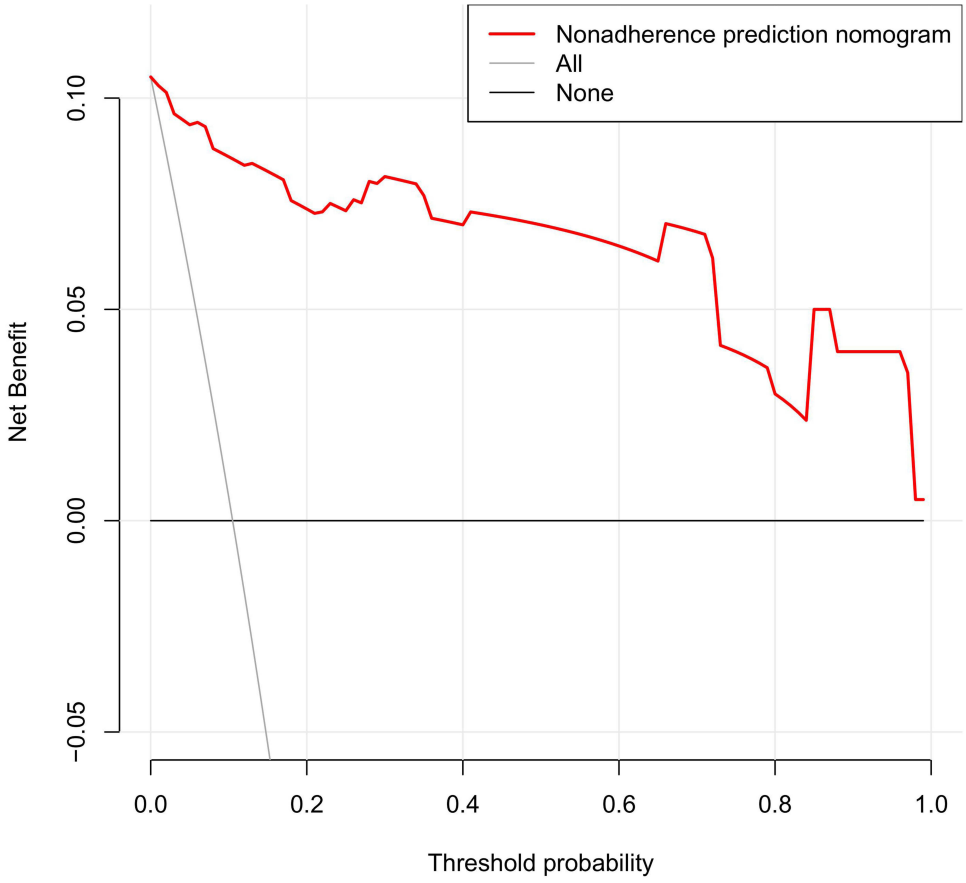

Figure 6 Decision analysis curves for nomogram models.

Discussion

With the development of molecular biotechnology, some scholars have pointed out that the pathogenesis of breast cancer involves the participation of a variety of proteins and plays a key role in the process of tumor development.[11] This study found that the high expression of THRSP and ACACA proteins was related to the clinical pathology and survival rate of breast cancer patients, and a nomogram model for the prognosis of breast cancer patients was constructed based on the expression levels of THRSP and ACACA.

https://doi.org/10.2147/PGPM.S516843

The results of this study found that the expression of THRSP and ACACA proteins in tumor tissues is related to lymph node metastasis. In addition, Cox regression analysis showed that high expression of THRSP and ACACA proteins was a risk factor affecting the prognosis of breast cancer patients, suggesting that THRSP and ACACA proteins may be related to disease progression. During the occurrence and development of breast cancer, the transformation of the metabolic model of cancer cells has led to a sharp increase in the demand for fatty acids.[12] High expression of THRSP and ACACA proteins helps cancer cells reshape the fat metabolic pathway and provide sufficient fatty acid raw materials for their rapid proliferation., thereby promoting the progress of the disease.[13,14] THRSP is a thyroid hormone-responsive protein, and under normal conditions, the expression of THRSP is strictly regulated by thyroid hormones, which plays an important role in maintaining the balance of fat metabolism in the body.[15] Abnormal expression of THRSP protein provides strong support for tumor cell growth by altering the metabolic pathway of breast cancer cells. On the one hand, THRSP protein provides a rich source of energy for tumor cells by promoting fatty acid synthesis;[16] on the other hand, THRSP proteins can also affect the proliferation and apoptosis balance of tumor cells by regulating cell cycle and apoptosis pathways.[17] Hu et al[18] reported that THRP plays a broad amplifying role in breast cancer, and high expression of THRP has been shown to predict the time to recurrence of breast cancer. Its higher expression is associated with lower expression of recurrence-free survival. ACACA protein can catalyze the conversion of acetyl-CoA to malonyl-CoA, thereby participating in the synthesis of fatty acids.[19] Overexpression of ACACA protein leads to activation of fatty acid synthesis pathways, thereby increasing the energy supply and biosynthetic capabilities of tumor cells, making tumor cells more aggressive and metastatic. Previous studies have found[20] that in breast cancer cells, the expression level of ACACA protein is usually high. Due to the enhanced activity of ACACA protein, breast cancer cells can synthesize more fatty acids, thus meeting their rapid proliferation and metastasis needs. In addition, Liu et al[21] reported that ACACA is highly expressed in prostate cancer, and its expression level is related to patient disease-free survival. All of the above studies indicated that ACACA protein expression may be closely related to the prognosis of breast cancer patients.

The Nomogram model is a visual graphical representation of a statistical prediction model that predicts the probability of clinical events by integrating different variables and has been widely used in clinical research in recent years.[22,23] The C-index is often used to assess the ability of models to distinguish between different outcomes. It is generally believed that when the value is greater than 0.7, the model has good discrimination. The C-index of the nomogram model constructed in this study is 0.704, indicating that this model has certain efficiency in distinguishing breast cancer patients with different prognosis. At the same time, the AUCs of the model predicting 1-year, 2-year and 3-year survival rates were 0.802, 0.769 and 0.770, respectively, indicating that the model has good accuracy in predicting patient survival rates at different time points after surgery. Clinicians can use this model to reliably estimate patient survival probability and provide strong data support for formulating personalized treatment plans.

The nomogram model based on the expression of THRSP and ACACA proteins constructed in this study brings new perspectives and tools to evaluate the prognosis of breast cancer patients. The advantage of this model is that it integrates the expression information of key proteins related to tumor metabolism, makes up for the shortcoming of traditional prognostic assessment relying only on clinical pathological factors, and improves the accuracy and comprehensiveness of prediction. Clinicians can quickly obtain predicted survival rates at different time points by inputting information such as patient TNM stage, lymph node metastasis, Ki-67 expression, THRSP and ACACA protein expression. Therefore, this model may help to more accurately predict patient prognosis and formulate reasonable treatment plans.

However, this study also has certain shortcomings. First of all, the distribution of breast cancer patients who meet the inclusion criteria of this study is relatively scattered and it is difficult to collect large numbers in a short period of time, resulting in possible insufficient case collection. In the future, multi-center cooperation can be adopted to collect cases. By cooperating with multiple hospitals, we will broaden the source channels of cases and increase the sample size. Second, this study did not include classic prognostic factors such as ER, PR, and HER2. THRSP and ACACA, as proteins related to lipid metabolism, may affect the progression of breast cancer through mechanisms independent of classical signaling pathways, such as lipid metabolic reprogramming. Future research should further optimize the model by combining multi-omic data (such as transcriptome and metabolome) and explore the potential synergy between THRSP and ACACA proteins and ER, PR, and HER2. In addition, for the nomogram model, this study lacks external verification based on other populations, and its universality still needs further verification.

Conclusion

In conclusion, nomogram based on clinical pathological characteristics and THRSP protein and ACACA protein is expected to become an effective tool for prognosis assessment of breast cancer patients. Monitoring the expression levels of THRSP and ACACA proteins in breast cancer tissue has positive clinical significance for assessing patient prognosis and formulating individualized treatment plans.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 helsinki declaration and its later amendments or comparable ethical standards.

This study was approved by The Ethics Committee of the First People's Hospital of Lianyungang.

Consent to Participate

Informed consent was obtained from every human participant in the study and the patients participating in the study all agree to publish the research results.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Wilkinson L, Gathani T. Understanding breast cancer as a global health concern. *Br J Radiol*. 2022;95(1130):20211033. doi:10.1259/bjr.20211033
2. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2021. *CA Cancer J Clin*. 2021;71(1):7–33. doi:10.3322/caac.21654
3. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209–249. doi:10.3322/caac.21660
4. Dore M, Faya N, Filoche S, Henry C. Transcriptomic identification of differentially expressed genes in Levonorgestrel resistant endometrial cancer cell lines. *Mol Carcinog*. 2023;62(7):1038–1050. doi:10.1002/mc.23544
5. Ding Y, Liu X, Yuan Y, et al. THRSP identified as a potential hepatocellular carcinoma marker by integrated bioinformatics analysis and experimental validation. *Aging*. 2022;14(4):1743–1766. doi:10.18632/aging.203900
6. Bacci M, Lorito N, Smiriglia A, et al. Acetyl-CoA carboxylase 1 controls a lipid droplet-vulnerability of endocrine-resistant ER(+) breast cancer. *Sci Trans Med*. 2024;16(736):eadf9874. doi:10.1126/scitranslmed.adf9874
7. Peng Y, Zhang X, Wu J, Wang H, Huang X. Development and validation of a Nomogram to predict postoperative flap necrosis risk in breast cancer patients undergoing modified radical mastectomy. *Am J Cancer Res*. 2025;15(3):1291–1306. doi:10.62347/DYFF7059
8. Huang X, Luo Z, Liang W, et al. Survival nomogram for young breast cancer patients based on the SEER database and an external validation cohort. *Ann Surg Oncol*. 2022;29(9):5772–5781. doi:10.1245/s10434-022-11911-8
9. Sciaraffa T, Guido B, Khan SA, Kulkarni S. Breast cancer risk assessment and management programs: a practical guide. *Breast J*. 2020;26 (8):1556–1564. doi:10.1111/tbj.13967
10. Teichgraeber DC, Guirguis MS, Whitman GJ. Breast cancer staging: updates in the AJCC cancer staging manual, 8th Edition, and current challenges for radiologists, from the AJR special series on cancer staging. *AJR Am J Roentgenol*. 2021;217(2):278–290. doi:10.2214/AJR.20.25223
11. Haykal MM, Rodrigues-Ferreira S, Nahmias C. Microtubule-Associated Protein ATIP3, an emerging target for personalized medicine in breast cancer. *Cells*. 2021;10(5):1080. doi:10.3390/cells10051080
12. Yao Y, Cai X, Fei W, et al. The role of short-chain fatty acids in immunity, inflammation and metabolism. *Crit Rev Food Sci Nutr*. 2022;62(1):1–12. doi:10.1080/10408398.2020.1854675
13. Tan K, Owen T, McEwen HP, et al. Acetyl-CoA carboxylase 1-dependent lipogenesis drives breast cancer progression. *J BioRxiv*. 2023;7 (2):549828.
14. Polasik D, Golińczak J, Proskura W, Terman A, Dybus A. Association between THRSP gene polymorphism and fatty acid composition in milk of dairy cows. *Animals*. 2021;11(4):1144. doi:10.3390/ani11041144
15. Yu ZX, Xiang C, Xu SG, Zhang YP. The clinical significance of thyroid hormone-responsive in thyroid carcinoma and its potential regulatory pathway. *Medicine*. 2022;101(31):e29972. doi:10.1097/MD.0000000000029972
16. Ke X, Zhang R, Li P, et al. Hydrochloride Berberine ameliorates alcohol-induced liver injury by regulating inflammation and lipid metabolism. *Biochem Biophys Res Commun*. 2022;610:49–55.
17. Ni Y, Hu Y, Lou X, et al. Spermidine ameliorates nonalcoholic steatohepatitis through thyroid hormone-responsive protein signaling and the gut microbiota-mediated metabolism of bile acids. *J Agric Food Chem*. 2022;70(21):6478–6492. doi:10.1021/acs.jafc.2c02729

18. Hu Q, Ma X, Li C, et al. Downregulation of THRSP promotes hepatocellular carcinoma progression by triggering ZEB1 transcription in an ERK-dependent manner. *J Cancer*. 2021;12(14):4247–4256. doi:10.7150/jca.51657
19. Huang YC, Hou M-F, Tsai Y-M, et al. Involvement of ACACA (acetyl-CoA carboxylase α) in the lung pre-metastatic niche formation in breast cancer by senescence phenotypic conversion in fibroblasts. *Cell Oncol*. 2023;46(3):643–660. doi:10.1007/s13402-022-00767-5
20. Hunt EG, Hurst KE, Riesenberg BP, et al. Acetyl-CoA carboxylase obstructs CD8(+) T cell lipid utilization in the tumor microenvironment. *Cell Metab*. 2024;36(5):969–983.e910. doi:10.1016/j.cmet.2024.02.009
21. Liu S, Lai J, Feng Y, et al. Acetyl-CoA carboxylase 1 depletion suppresses de novo fatty acid synthesis and mitochondrial β-oxidation in castration-resistant prostate cancer cells. *J Biol Chem*. 2023;299(1):102720. doi:10.1016/j.jbc.2022.102720
22. Zheng P, Lai C, Yang W, et al. Nomogram predicting cancer-specific survival in elderly patients with stages I-III colon cancer. *Scand J Gastroenterol*. 2020;55(2):202–208. doi:10.1080/00365521.2020.1720280
23. Liu J, Huang X, Yang W, et al. Nomogram for predicting overall survival in stage II-III colorectal cancer. *Cancer Med*. 2020;9(7):2363–2371. doi:10.1002/cam4.2896