The predictive value of tumor-to-gland density ratio in pathological complete response to neoadjuvant chemotherapy in breast cancer

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Abstract

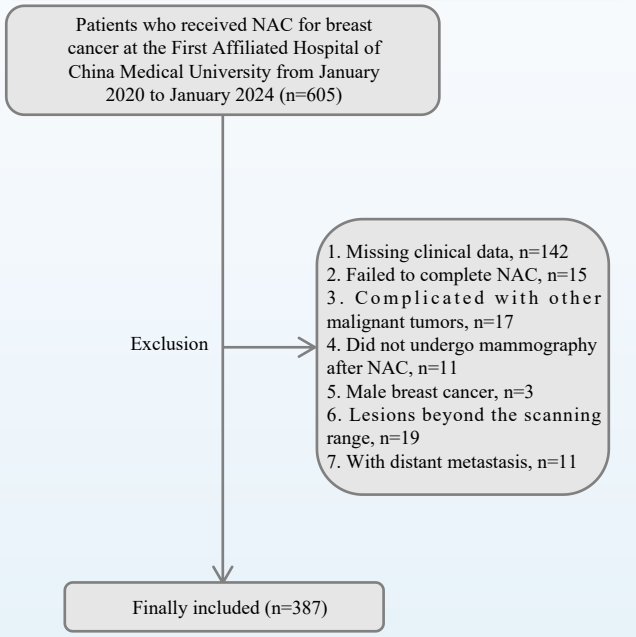
Purpose: To construct a predictive model incorporating an innovative imaging index (primary breast cancer lesion/glandular density ratio) for neoadjuvant chemotherapy (NAC) in breast cancer, optimize personalized treatment decisions, and improve therapeutic efficacy and patients' quality of life.

Methods: A total of 387 breast cancer patients receiving NAC were enrolled. Clinicopathological data and imaging information were extracted. Key indicators (lesion/glandular density ratio, ER, HER2, Ki67) were screened via multiple regression analyses to build and validate a nomogram model, with a concurrent development of a visual prediction tool.

Results: The model achieved an AUC of 0.852, with reliable stability confirmed by Bootstrap validation (AUC=0.850). The novel imaging index significantly enhanced predictive performance, increasing the model's AUC from 0.769 to 0.852 (P<0.01) and showing a negative correlation with pathological complete response (pCR) (smaller ratio correlates with higher pCR rate).

Conclusion: The predictive model, constructed with the primary breast cancer lesion/glandular density ratio, ER, HER2, and Ki67, exhibits accurate prediction and excellent fitting. Notably, the primary breast cancer lesion/glandular density ratio serves as a crucial independent predictor of NAC efficacy, whose incorporation remarkably boosts the model's predictive efficiency.

Scheme



Methods

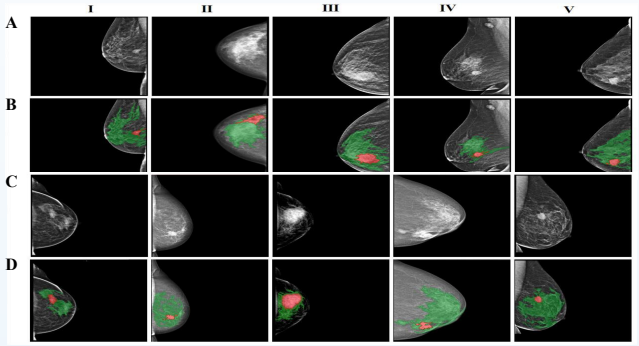


Figure 1. Comparison of pre-NAC original mammographic images and target volume delineation maps in breast cancer patients. A and C: Pre-NAC original mammographic images of patients; B and D: Pre-NAC mammographic images with target volume delineation of patients.

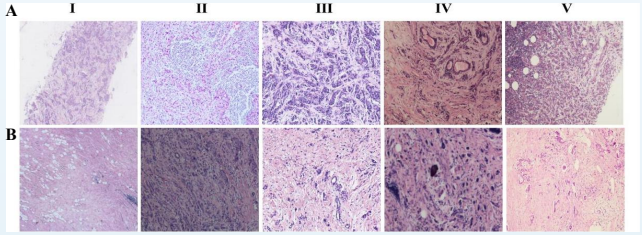


Figure 2. Comparison of pathological response classification (HE Staining, ×100). A: Pre-NAC pathological results of breast cancer patients; B: Post-NAC pathological results of breast cancer patients.

Conclusion

This study targeted breast cancer patients receiving NAC and built a predictive model integrating the primary breast cancer lesion/gland density ratio, ER, HER2, and Ki67 to enhance pCR prediction accuracy. The lesion/gland density ratio is an independent predictor of NAC efficacy, negatively correlated with pCR and significantly boosting model performance—with marked drops when this ratio is excluded. The model, proven stable and clinically valuable, was converted into a nomogram and visual application, offering a practical tool for personalized chemotherapy planning.

Prospect

In the future, we will expand the research depth and application scope from multiple dimensions to further unlock the research value:

1. Expand the sample size and conduct multi-center validation to improve the applicability and stability of the model in different clinical scenarios and enhance its external validity.
2. Combine technologies such as tumor microenvironment detection and gene sequencing to explore the core molecular mechanisms and provide theoretical support for targeted intervention.
3. Conduct subgroup analysis for different molecular subtypes of breast cancer, clarify the differences in the predictive efficacy of the density ratio among various subtypes, and formulate subtype-specific prediction and treatment strategies.
4. Optimize the visual prediction application by adding a dynamic monitoring module, which integrates imaging review data during chemotherapy to realize real-time efficacy evaluation and dynamic adjustment of treatment plans, thereby improving clinical practicality.

Results

Table 1. Multivariate logistic stepwise regression analysis for NAC efficacy prediction

Variable	β	SE	Z	P	OR (95%CI)
Density	-6.50218	1.01810	-6.387	0.00013	0.0014 (0.0002, 0.0078)
ER-Positive	-0.72677	0.27280	-2.664	0.00772	0.32157 (0.21010, 0.48806)
HER2-Positive	1.19437	0.38504	3.102	0.00192	6.65860 (4.29091, 10.48681)
Ki67-High expression	1.34279	0.51383	2.613	0.00897	7.05488 (3.12673, 18.93994)
HER2-targeted Chemotherapy	0.66547	0.38803	1.715	0.08635	6.51097 (4.13386, 10.42086)

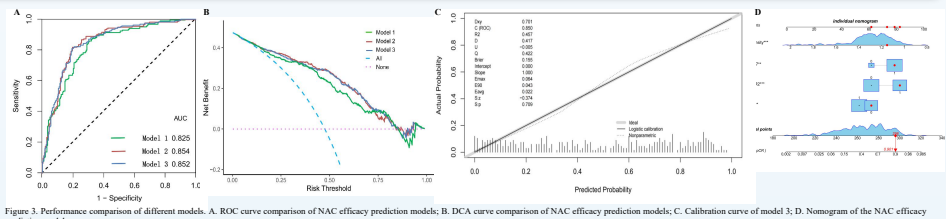


Figure 3. Performance comparison of different models. A. ROC curve comparison of NAC efficacy prediction models; B. DCA curve comparison of NAC efficacy prediction models; C. Calibration curve of model 3; D. Nomogram of the NAC efficacy prediction model.

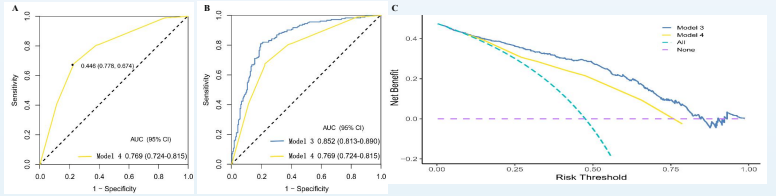


Figure 4. Predictive value of primary breast cancer lesion/glandular density ratio for NAC efficacy. A and B: ROC curve comparison between model 3 and model 4; C: DCA curve comparison between model 3 and model 4.



Figure 5. Predictive application for NAC efficacy (https://hongruiwei.shinyapps.io/dynnomapp/)