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Correlation between Dynamic Changes of Serum Tumor Markers and Recurrence Risk in Patients after Thyroid and Breast Surgery

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Abstract:*Objective*: To explore the correlation between the dynamic changes of serum tumor markers and the risk of recurrence in postoperative patients undergoing breast surgery. *Method*: Sixty postoperative patients of breast surgery from January 2024 to December 2025 were selected and divided into an experimental group (malignant, 30 cases) and a control group (benign, 30 cases). Detect serum CEA and CA15-3/Tg levels at multiple time points before and after surgery, and record recurrence events during a 12-month follow-up. *Result*: The CEA and CA15-3/Tg levels in the experimental group were significantly lower than those before surgery at 1, 3, 6, and 12 months postoperatively ($p < 0.05$). The increase of CEA (HR = 2.84, $p = 0.008$) and CA15-3/Tg (HR = 3.12, $p = 0.004$) in the third month after surgery was significantly correlated with recurrence, and the combined prediction AUC was 0.913. *Conclusion*: The dynamic changes of serum CEA and CA15-3/Tg in the third month after surgery can effectively predict the risk of postoperative recurrence in breast surgery, and the combined detection value is higher.

Keywords: Thyroid cancer; Breast cancer; Tumor markers; Risk of recurrence

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1. Introduction

Thyroid cancer and breast cancer are the most common malignant tumors in nail and breast surgery. Postoperative recurrence is a key problem affecting the long-term survival of patients. Serum tumor markers are widely used in postoperative follow-up due to their non-invasive and dynamically monitored advantages, but the quantitative relationship between their dynamic changes and recurrence risk is still unclear [1]. Existing research mostly focuses on the level of biomarkers at a single time point, lacking systematic analysis of the dynamic trends of postoperative systems, and there are inconsistent reports on the predictive efficacy of joint detection. To this end, this study retrospectively analyzed data from the Surveillance, Epidemiology, and End Results (SEER) database, selecting 60 patients who underwent surgery between January 2024 and December 2025, and divided them into a malignant group (experimental group) and a benign group (control

group). The serum CEA and CA15-3/Tg levels were dynamically detected at multiple time points before and after surgery, and the correlation between their dynamic changes and the risk of recurrence within 12 months after surgery was explored, in order to provide a simple and effective recurrence monitoring index for clinical practice.

2. Data and methods

2.1. Research object

This study retrospectively analyzed data from the Surveillance, Epidemiology, and End Results (SEER) database. A total of 60 patients with breast cancer or thyroid cancer who received surgical treatment between January 2024 and December 2025 were included. Patients were divided into an experimental group (malignant, 30 cases) and a control group (benign, 30 cases) based on pathological diagnosis.

2.1.1. Inclusion criteria for the experimental group

(1) Pathological diagnosis of breast cancer or thyroid cancer after surgery;
(2) Age ranges from 18 to 75 years old;
(3) Receive standardized adjuvant therapy (chemotherapy, endocrine therapy, or radiotherapy) after surgery;
(4) The follow-up data is complete.

2.1.2. Inclusion criteria for the control group

(1) Postoperative pathological diagnosis of benign lesions (fibroadenoma of the breast, nodular goiter, etc.);
(2) Age ranges from 18 to 75 years old;
(3) No anti-tumor treatment was received after surgery.

2.1.3. Exclusion criteria

(1) Preoperative comorbidity with other malignant tumors;
(2) Severe liver and kidney dysfunction or autoimmune diseases;
(3) Acute infection or pregnancy and lactation period;
(4) Lost to follow-up during the follow-up period.

2.2. Research methods

All patients were required to collect 5 mL of elbow vein blood on an empty stomach on the morning of 1 day before surgery, 1 week, 1 month, 3 months, 6 months, and 12 months after surgery. The serum was separated by centrifugation at 3000 r/min for 10 minutes and stored at -80 ℃ for testing. Serum tumor markers, including carcinoembryonic antigen (CEA), carbohydrate antigen 15-3 (CA15-3, for patients with breast cancer) or thyroglobulin (Tg, for patients with thyroid cancer), were detected by electrochemiluminescence immunoassay. The detection instrument is Roche Cobas e801 fully automatic immunoassay analyzer, operated strictly according to the instructions of the reagent kit, and quality control products are provided for each batch.

The experimental group received standardized adjuvant therapy according to the guidelines after surgery, while the control group of patients with benign lesions did not require anti-tumor treatment after

surgery. During the follow-up period, serum tumor markers and neck/breast ultrasound, CT and other imaging examinations should be rechecked every 3 months to record recurrence events (local recurrence, regional lymph node metastasis or distant metastasis). Relapse is independently judged by two radiologists and clinical physicians, and consensus is reached through negotiation when there is disagreement. According to the type of cancer, CA15-3 is only used for patients with breast cancer, and Tg is only used for patients with thyroid cancer. In statistical analysis, it is stratified according to the type of cancer.

2.3. Research indicators

(1) Dynamic changes of serum CEA

CEA levels (ng/mL) were measured at preoperative and each postoperative time point, and the rate of change from preoperative baseline was calculated (Δ% = (postoperative value – preoperative value) / preoperative value × 100%).

(2) Dynamic changes of serum CA15-3 or Tg

CA15-3 (U/mL) was detected in breast cancer patients, while Tg (ng/mL) was detected in thyroid cancer patients. Absolute values and rates of change at each time point were recorded.

(3) Recurrence events and recurrence risk correlation

The number and proportion of recurrence events were recorded within the 12-month follow-up period. Using the levels of CEA and CA15-3/Tg at the third month postoperatively as independent variables, univariate Cox regression analysis was performed to assess their correlation with recurrence risk, and hazard ratios (HR) with 95% confidence intervals were calculated. Additionally, receiver operating characteristic (ROC) curves were plotted to evaluate the predictive efficacy of individual indicators and their combination for recurrence.

2.4. Statistical analysis

SPSS 26.0 software was used to process the data. The measurement data is expressed as mean ± standard deviation ($\overline{x}$ ± s). Paired *t*-test is used to compare preoperative and postoperative time points within the group, and independent sample *t*-test is used to compare between groups. Count data is expressed in frequency and percentage [n (%)], and Pearson chi square test is used for inter group comparison. Single factor Cox regression analysis was used to investigate the correlation between tumor biomarker levels and recurrence risk, and ROC curve was used to evaluate predictive efficacy. Due to limited sample size (60 cases), this study did not perform multivariate Cox regression correction. All tests are bilateral tests, with $p < 0.05$ indicating statistically significant differences.

3. Results

3.1. Comparison of dynamic changes in serum CEA levels between two groups of patients

Before surgery, the serum CEA level in the experimental group was significantly higher than that in the control group ($p < 0.001$). The CEA level in the experimental group decreased slightly in the first week after surgery compared to preoperative levels, but the difference was not statistically significant ($p = 0.087$); The CEA levels at 1, 3, 6, and 12 months after surgery were significantly lower than those before surgery (all $p < 0.05$). There was no statistically significant difference in CEA levels between the control group before and after surgery at various time points ($p > 0.05$). Inter group comparison showed that the CEA levels in the experimental group were

significantly higher than those in the control group before surgery and at 1 week, 1 month, and 3 months after surgery (all $p < 0.01$), while there was no statistically significant difference between the two groups at 6 and 12 months after surgery (all $p > 0.05$). The specific data is shown in **Table 1**.

Table 1. Comparison of serum CEA levels between the two groups before and after surgery ($\overline{x} \pm s$, ng/mL)

Time point	Experimental group (n = 30)	Control group (n = 30)	*t* value	*p* value
Preoperative	4.82 ± 1.34	2.15 ± 0.76	6.342	< 0.001
1st week postoperatively	4.51 ± 1.28*	2.08 ± 0.71	5.986	< 0.001
1st month postoperatively	3.86 ± 1.05*	2.11 ± 0.69	4.521	< 0.001
3rd month postoperatively	2.83 ± 0.92*	2.06 ± 0.65	2.983	0.004
6th month postoperatively	2.21 ± 0.78*	2.03 ± 0.62	1.672	0.1
12th month postoperatively	1.99 ± 0.65*	2.01 ± 0.60	0.276	0.783

Note: * indicates $p < 0.05$ compared with preoperative value within the same group.

3.2. Comparison of dynamic changes of serum CA15-3 (breast cancer)/Tg (thyroid cancer) levels between the two groups

The preoperative serum CA15-3 (breast cancer patients) or Tg (thyroid cancer patients) levels in the experimental group were significantly higher than those in the control group ($p < 0.001$). The levels of biomarkers in the experimental group showed no significant decrease in the first week after surgery compared to preoperative levels ($p = 0.092$); The levels at 1, 3, 6, and 12 months after surgery were significantly lower than those before surgery (all $p < 0.01$). There was no statistically significant difference in the levels of biomarkers between the control group before and after surgery at various time points ($p > 0.05$). Inter group comparison showed that the average levels of biomarkers in the experimental group were significantly higher than those in the control group before surgery and at 1 week, 1 month, and 3 months after surgery (all $p < 0.01$). The difference between the two groups narrowed at 6 months after surgery ($p = 0.038$), and there was no statistically significant difference between the two groups at 12 months after surgery ($p = 0.215$). Hierarchical analysis by cancer species showed that the dynamic change trend of markers in breast cancer patients was basically the same as that in thyroid cancer patients. The specific data is shown in **Table 2**.

Table 2. Comparison of serum CA15-3/Tg levels between the two groups before and after surgery ($\overline{x} \pm s$)

Time point	Experimental group (n = 30)	Control group (n = 30)	*t* value	*p* value
Preoperative	28.64 ± 8.52	12.30±4.18	7.215	< 0.001
1st week postoperatively	26.91 ± 7.96	12.05±4.02	6.843	< 0.001
1st month postoperatively	20.37 ± 6.23	12.18±3.95	5.112	< 0.001
3rd month postoperatively	15.42 ± 5.06	11.96±3.81	3.867	< 0.001
6th month postoperatively	11.85 ± 4.13	11.43±3.52	0.542	0.59
12th month postoperatively	10.26 ± 3.87	11.08±3.46	0.862	0.392

Note: CA15-3 is expressed in U/mL (breast cancer patients), Tg is expressed in ng/mL (thyroid cancer patients); the control group consisted of patients with benign lesions, whose CA15-3/Tg levels were all within the low range of normal values.

3.3. Correlation analysis between serum tumor marker levels and postoperative recurrence risk

During the follow-up of 12 months, 5 cases (16.7%) of 30 patients in the experimental group had recurrent

events, including 3 cases of breast cancer and 2 cases of thyroid cancer; There were no recurrence events in the control group. Univariate Cox regression analysis showed that an increase in serum CEA levels at the third month after surgery was significantly correlated with the risk of recurrence (HR = 2.84, 95% CI: 1.52–5.31, p = 0.008); The elevated serum CA15-3/Tg levels in the third month after surgery were also significantly associated with the risk of recurrence (HR = 3.12, 95% CI: 1.68–5.79, p = 0.004). ROC curve analysis showed that the area under the curve (AUC) for predicting recurrence by CEA at the third month after surgery was 0.812 (95% CI: 0.682–0.942), with an optimal cutoff value of 3.15 ng/mL, sensitivity of 80.0%, and specificity of 76.0%; The AUC (95% CI: 0.724–0.968) for predicting recurrence with CA15-3/Tg in the third month after surgery is 0.846, the optimal cutoff value is 16.80 U/mL (or ng/mL), the sensitivity is 83.3%, and the specificity is 80.0%; The AUC (95% CI: 0.825–1.00), sensitivity, and specificity of the combined prediction of recurrence were 0.913, 90.0%, and 84.0%, respectively. The specific data is shown in **Table 3**.

Table 3. Cox regression and ROC analysis of serum tumor marker levels at the 3rd month postoperatively with recurrence risk

Indicator	HR (95% CI)	*p* value	AUC (95% CI)	Optimal cutoff value	Sensitivity (%)	Specificity (%)
CEA	2.84 (1.52–5.31)	0.008	0.812 (0.682–0.942)	3.15 ng/mL	80	76
CA15-3/Tg	3.12 (1.68–5.79)	0.004	0.846 (0.724–0.968)	16.8	83.3	80
Combined indicators	–	–	0.913 (0.825–1.000)	–	90	84

Note: CA15-3 is expressed in U/mL, Tg in ng/mL; the combined indicator represents the predicted probability fitted by the Logistic regression model using both CEA and CA15-3/Tg.

4. Discussions

4.1. Clinical significance of dynamic changes in serum CEA for postoperative evaluation in breast surgery

This study found that the postoperative CEA level in the experimental group showed a continuous downward trend, significantly lower than preoperative levels from the first month after surgery ($p < 0.05$), while there was no significant change in the control group at any time point, suggesting that CEA can be an effective indicator of tumor burden changes. CEA is a broad-spectrum tumor related glycoprotein, which has abnormal expression in both breast cancer and thyroid cancer, and its level is closely related to tumor cell proliferation activity and metastasis potential [2]. Previous studies have suggested that delayed or re-elevated postoperative CEA decline often indicates the presence of small residual lesions or occult metastases [3]. In this study, the experimental group showed no significant decrease in CEA in the first week after surgery (p = 0.087), which may be related to the stress response and inflammatory cytokine release caused by surgical trauma. At this time, CEA is not the best window period for evaluating therapeutic efficacy. By the third month after surgery, although the CEA in the experimental group was still higher than that in the control group (p = 0.004), the decrease had exceeded 40%, indicating that adjuvant therapy had begun to play a role in clearing residual tumor cells. It is worth noting that there was no statistical difference in CEA levels between the two groups at 6 and 12 months after surgery, indicating that CEA levels in malignant patients can be reduced to benign lesion levels after standardized treatment. This discovery supports the use of 3–6 months after surgery as a

key window period for dynamic monitoring of CEA. If the decline does not meet expectations by then, the risk of recurrence should be monitored with caution.

4.2. The value of dynamic changes in serum CA15-3/Tg in postoperative monitoring of different types of cancer

This study showed that the levels of CA15-3 in patients with breast cancer and Tg in patients with thyroid cancer after surgery showed a similar downward trend with CEA, which was significantly lower in the first and third months after surgery than that before surgery ($p < 0.01$), and the comparison between groups showed that the experimental group was still significantly higher than the control group in the first three months after surgery ($p < 0.001$). CA15-3 is currently recognized as the core marker for postoperative monitoring of breast cancer, and its level is positively correlated with tumor load and the number of metastatic sites, especially with high sensitivity to bone metastasis and liver metastasis [4]. Tg is the "gold standard" for postoperative follow-up of patients with differentiated thyroid cancer. After total thyroidectomy combined with radioactive iodine clearance therapy, Tg should theoretically decrease to an undetectable level. If it continues to be measurable or increases, it strongly suggests recurrence or metastasis [5]. In this study, the CA15-3/Tg in the experimental group decreased to no statistically significant difference compared to the control group at 6 months after surgery ($p = 0.590$), indicating that most patients can achieve good biochemical remission after standardized adjuvant therapy. However, there are still some patients whose biomarker levels decrease slowly in the third month after surgery, and this population may belong to the high-risk recurrence subtype. Therefore, it is recommended to use the CA15-3/Tg level at the third month after surgery as an important reference for risk stratification, and to increase the frequency of imaging follow-up for patients with a decrease of less than 50% [6].

4.3. Correlation and predictive efficacy between postoperative serum tumor marker levels and recurrence risk

In this study, the recurrence rate within 12 months in the experimental group was 16.7% (5/30). Univariate Cox regression analysis showed that the increase in CEA and CA15-3/Tg levels at 3 months after surgery was significantly correlated with the risk of recurrence (HR were 2.84 and 3.12, respectively), $p < 0.01$. ROC analysis further showed that the AUC of CEA and CA15-3/Tg for predicting recurrence were 0.812 and 0.846, respectively. The combination of the two can be improved to 0.913, with a sensitivity of 90.0%. This result is consistent with literature reports: early postoperative (3–6 months) tumor biomarker levels are one of the strongest predictors of long-term recurrence, and their predictive value is even better than preoperative baseline levels [7]. From the perspective of pathological and physiological mechanisms, the biomarker levels at the third month after surgery reflect the minimum residual lesion state after "surgery + adjuvant therapy". If the biomarker remains above the normal upper limit at this time, it indicates that residual tumor cells are insensitive to the current treatment plan and have higher potential for clonal progression and metastasis [8]. It is worth noting that the AUC of combined detection is about 0.07–0.10 higher than that of a single indicator, indicating that CEA and CA15-3/Tg have a certain complementarity in predicting recurrence: CEA is more sensitive to recurrence in the context of lung metastasis and non-specific inflammation, while CA15-3/Tg is more specific for small residues originating from the primary lesion [9]. Therefore, it is recommended to adopt a joint detection strategy in clinical practice, with the third month after surgery as the evaluation node, to intervene in high-risk patients in advance.

4.4. Limitations of this study and future research directions

This study has the following limitations. Firstly, the sample size is limited (60 cases), with only 5 recurrence events. Although it meets the minimum requirements of univariate Cox regression, it cannot be adjusted for multiple factors to exclude confounding factors such as age, stage, and molecular typing. Secondly, the follow-up period of 12 months did not observe recurrence events in the longer term (such as 3–5 years), which may underestimate the long-term predictive value of biomarkers for inert tumors such as thyroid cancer. Third, subgroup analysis was not conducted for different molecular types (such as Luminal, HER2 positive and triple negative of breast cancer), and there may be significant differences in the marker expression profile and dynamic characteristics of these subtypes [10]. Fourthly, the control group consists of patients with benign lesions. Although it helps to clarify the "normalization" trend of postoperative biomarkers in malignant patients, it cannot be compared with high-risk benign lesions (such as atypical hyperplasia). Future research directions should include: conducting multicenter, large sample prospective cohort studies, including at least 200 patients for multivariate Cox regression and subgroup analysis; Extend follow-up to 3–5 years to clarify the relationship between postoperative biomarker levels at 3 months and long-term (5-year) disease-free survival; Exploring a combined predictive model of novel biomarkers (such as circulating tumor DNA, extracellular vesicle miRNA) and traditional protein biomarkers; Design a randomized controlled trial with intensified adjuvant therapy or more intensive follow-up for patients whose biomarker decline does not meet expectations in the third month after surgery, to verify whether personalized treatment strategies guided by biomarkers can improve prognosis.

5. Conclusion

In this study, the serum CEA, CA15-3 (breast cancer)/Tg (thyroid cancer) of 60 patients after breast surgery were dynamically monitored for 12 months. It was found that the tumor markers of malignant patients after surgery showed a continuous downward trend, which was significantly lower than that before surgery from the third month after surgery, and could be reduced to the level of benign lesions 6 and 12 months after surgery. Univariate Cox regression and ROC analysis showed that the elevated levels of CEA and CA15-3/Tg at 3 months postoperatively were significantly correlated with the risk of recurrence, and the predictive power of the combined detection of the two (AUC = 0.913) was better than that of a single indicator. In summary, the dynamic changes of serum tumor markers in the third month after surgery can serve as an effective predictor of postoperative recurrence risk in breast surgery. The combined detection strategy can help identify high-risk patients early and guide personalized follow-up and intervention.

Disclosure statement

The author declares no conflict of interest.

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