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Clinical Impact of CA15-3 and CEA Tumor Markers in Breast Cancer Management: A Retrospective Analysis

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Abstract:

Introduction: Breast cancer is the most common cancer in women, ahead of colorectal cancer and lung cancer. Among the protein substances or hormones produced by cancerous tissues are tumor markers such as CA15-3 and CEA, which are specific to breast cancer.

Materials and Methods: Our work consisted of conducting a retrospective clinical study at the Oncology Center of Relizane, covering the period from January 1, 2019, to December 31, 2022. This research focused on 470 cases of breast cancer, including 457 women and 13 men, with ages ranging from 22 to 90 years. The objective of this study was to evaluate the significance of tumor markers in the management of breast cancer.

Results and Discussion: Our investigation demonstrated that the predominant histological type was stage I and II carcinoma, with co-dominance between the involvement of the left and right breasts. The HER2+ molecular type was the most dominant in our study. Tumor marker results showed that the levels of CA15-3 and CEA were elevated in patients who had developed metastasis, with 89.19% and 32.96% of cases respectively. A statistically highly significant relationship was found between the development of metastasis and the levels of tumor markers CA15-3 and CEA (p=0.0001).

Conclusion: Tumor markers are a crucial tool for diagnosing the patient's condition, anticipating and monitoring an individual's response to certain treatments, and detecting cancer recurrence.

Keywords: Breast cancer, tumor markers, clinical aspects, CA15-3, ACE

1. Introduction

Breast cancer ranks first among prevalent cancer types in Algeria. According to the International Agency for Research on Cancer (IARC), the incidence of breast cancer in Algeria was approximately 12,532 cases (23.3%) in 2020 (IARC, 2020).

Substances involved in the carcinogenesis process are called tumor markers (Novakovic, 2004). These substances are secreted by cancer cells or by healthy tissues in response to the presence of a tumor. This molecular parameter is found on tumor tissue or in biological fluids such as blood and urine (Rigaud et al., 2002). Tumor markers may be expressed in various cancers or be specific to a particular tissue origin (Mohamed, 2010). Most tumor markers are proteins or glycoproteins (Carcinoembryonic Antigen "CEA," Cancer Antigen "CA15-3," Cancer Antigen "CA125," Alpha-fetoprotein "AFP," and, less commonly, hormones like "HCG, calcitonin") or enzymes such as Neuron-Specific Enolase "NSE" (Zenhausern, 2011).

2. Materials and Methods

Our study involved a retrospective clinical investigation at the Oncology Center in Relizane, covering the period from January 1, 2019, to December 31, 2022. This research included 470 breast cancer cases, distributed among 457 women and 13 men, with ages ranging from 22 to 90 years. The objective was to evaluate the significance of tumor markers in breast cancer management.

All data were collected from individual patient investigation forms, anatomopathological examination results, and analyses conducted in medical biology laboratories and at the Relizane Oncology Center. Blood samples were taken to measure plasma levels of tumor markers CA15-3 and CEA using the VIDAS analyzer based on the ELFA technique (ELISA with fluorescence endpoint reading).

Data entry and statistical analysis were performed using IBM SPSS Statistics software (version 21.0). Results were presented as histograms using Microsoft Office Excel 2007. Qualitative variables were expressed as percentages, while quantitative variables were presented as mean ± standard deviation. The Chi-square test was used

for comparing qualitative variables, with a p-value ≤ 0.05 considered statistically significant.

3. Results

3.1. Clinical Characteristics

3.1.1. Cancer Type:

Our analysis revealed that the right and left breasts were affected almost equally, with respective rates of 47.7% and 47.0%. However, bilateral involvement was observed in only 25 patients (5.3%) (Figure 1).

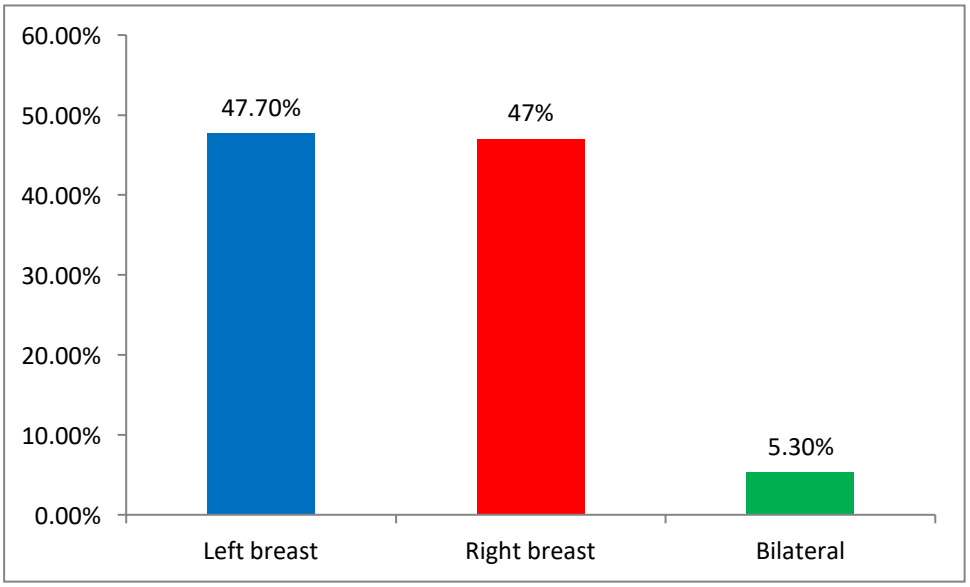

Figure 1: Distribution of patients by cancer type

3.1.2. Histological Type:

Histological analysis showed that carcinoma was predominant in 88.3% of breast cancer cases, followed by sarcoma in 11.7% (Figure 2).

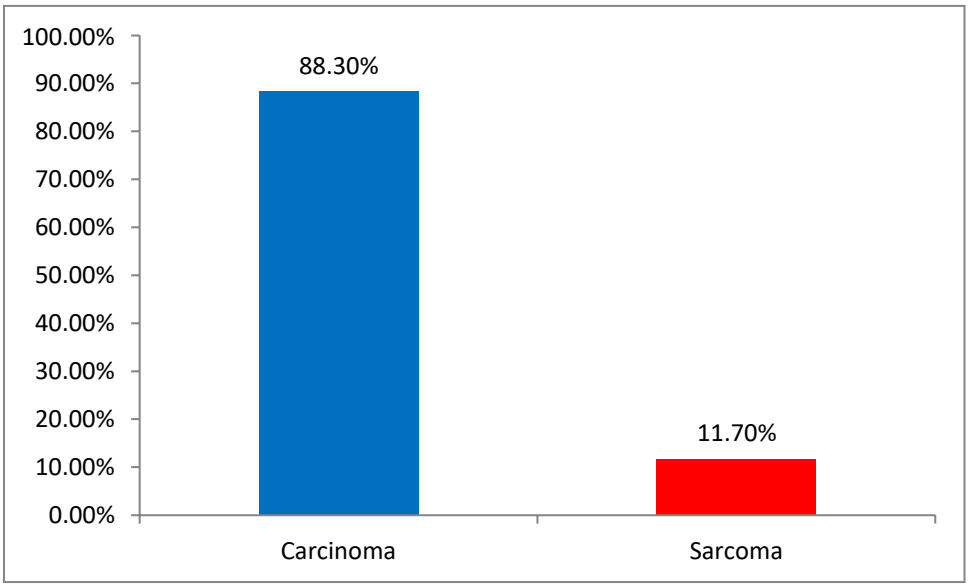

Figure 2: Histological distribution of breast cancer

3.1.3. Breast Cancer Stage:

The most common stage in our study was Stage I, observed in 240 patients (51.49%). Stages II, III, and IV were diagnosed in 38.09%, 8.51%, and 1.91% of cases, respectively (Figure 3).

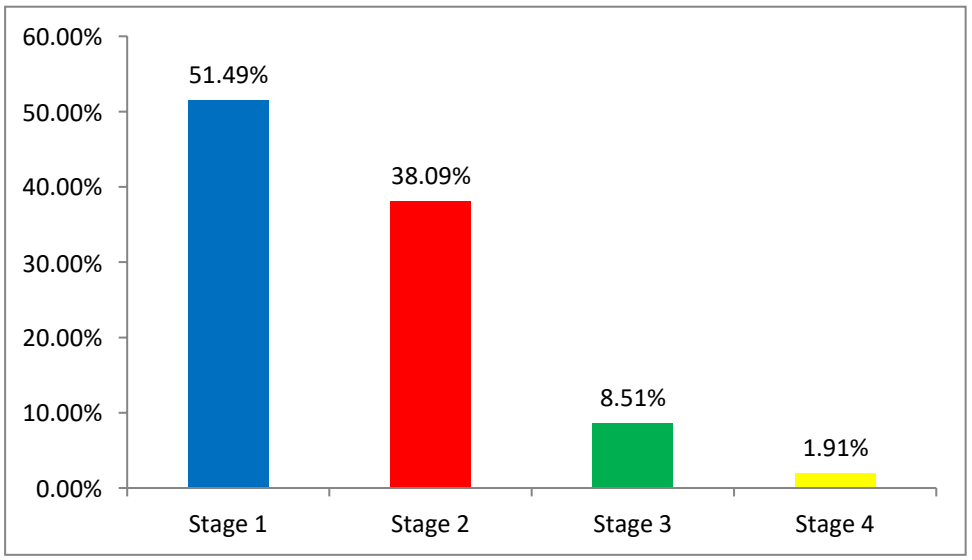

Figure 3: Distribution of patients by breast cancer stage

3.1.4. SBR Grades:

Grade II was the most frequent, observed in 218 patients (46.4%) (Figure 4), followed by Grade III (34.3%) and Grade I (19.4%).

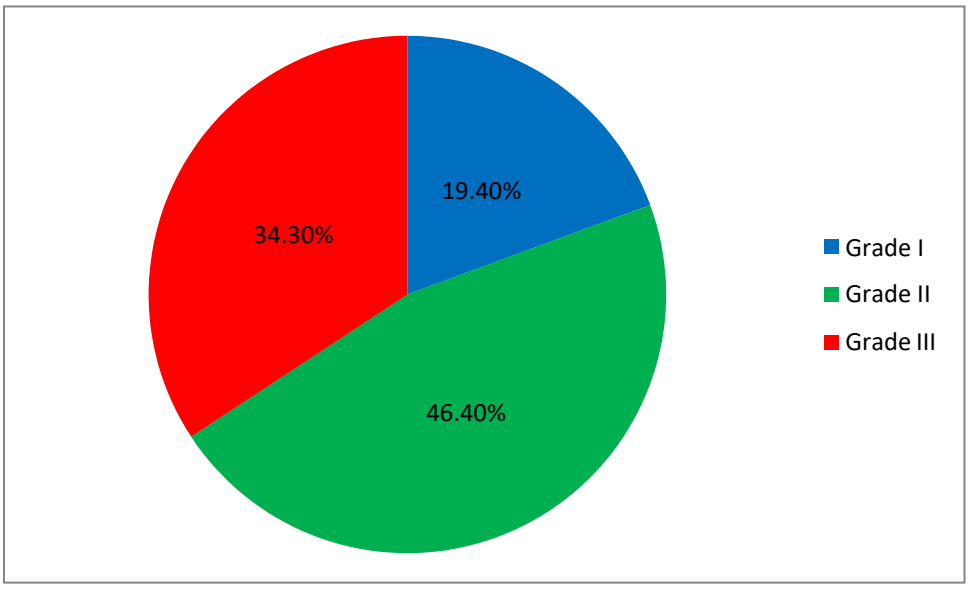

Figure 4: Distribution of patients by SBR grade

3.1.5. Mastectomy:

In our study, the mastectomy rate was 30.9% for the right breast and 35.0% for the left breast (Figure 5). However, in 30.5% of cases, this surgical procedure was not performed.

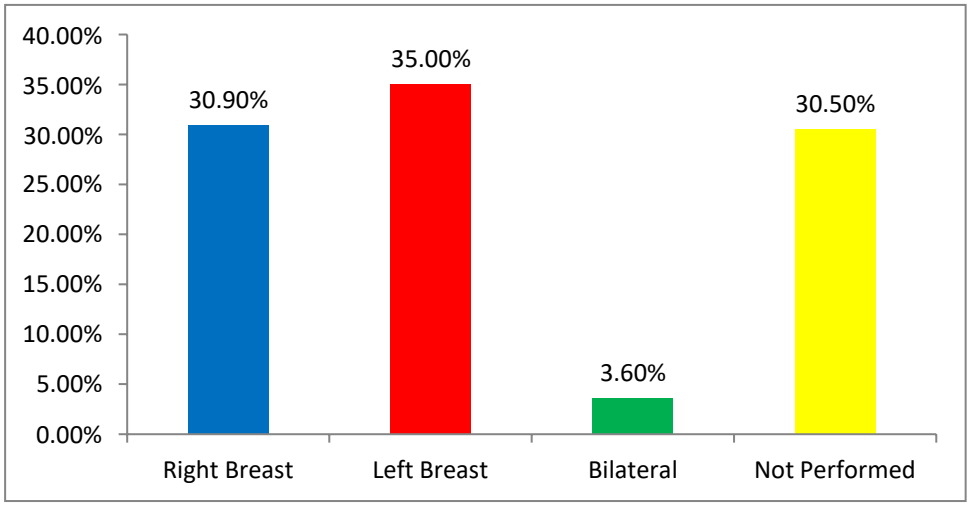

Figure 5: Distribution of patients by mastectomy

3.1.6. Molecular Subtypes:

We observed HER2 positivity in 57.4% of patients. The luminal A, luminal B, and

triple-negative subtypes were present in 17.01%, 19.25%, and 9.34% of cases, respectively (Figure 6).

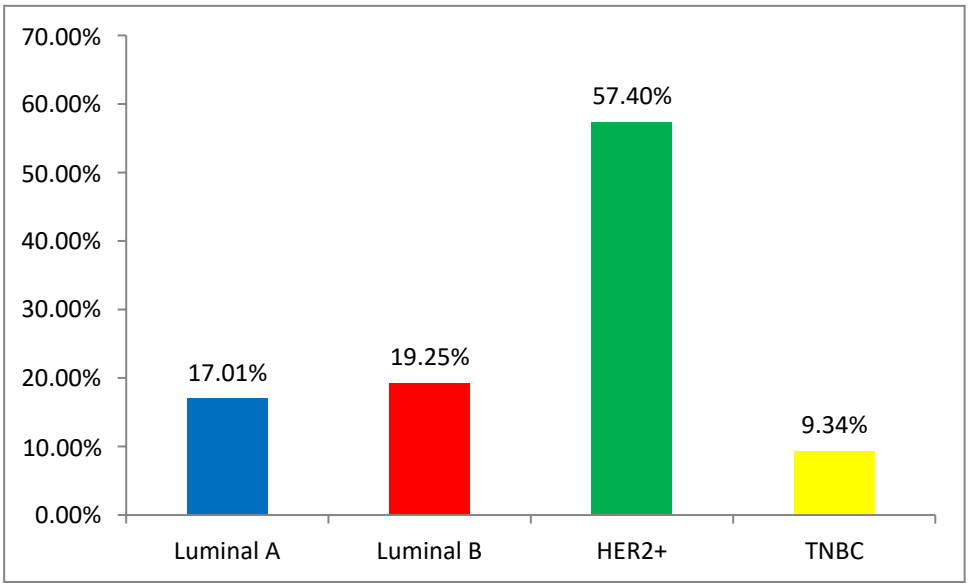

Figure 6: Distribution of breast cancers by molecular subtype

3.2. Tumor Markers

3.2.1. Biological Marker CA15-3:

CA15-3 analysis showed elevated levels in 39.27% of cases, low levels in 32.42%, and normal levels in 28.31% of patients (Figure 7).

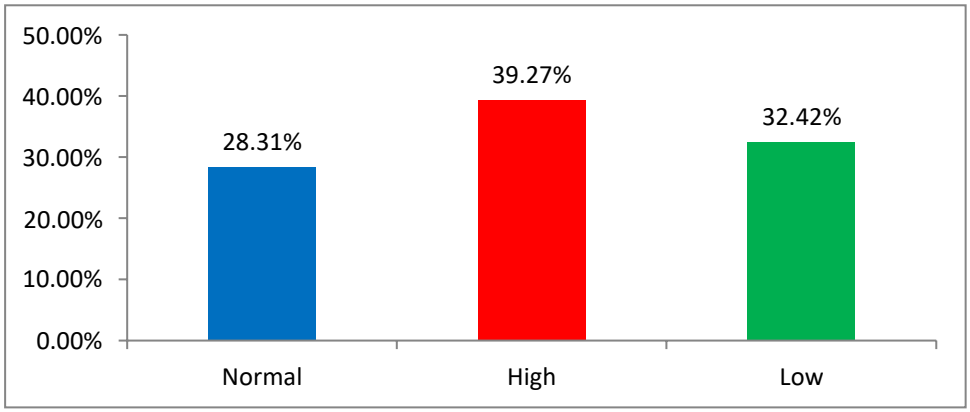

Figure 7: Distribution of patients by CA15-3 marker

3.2.2. Biological Marker CEA:

CEA analysis revealed low levels in 83.63% of cases, normal levels in 9.64%, and elevated levels in 6.73% of cases (Figure 8).

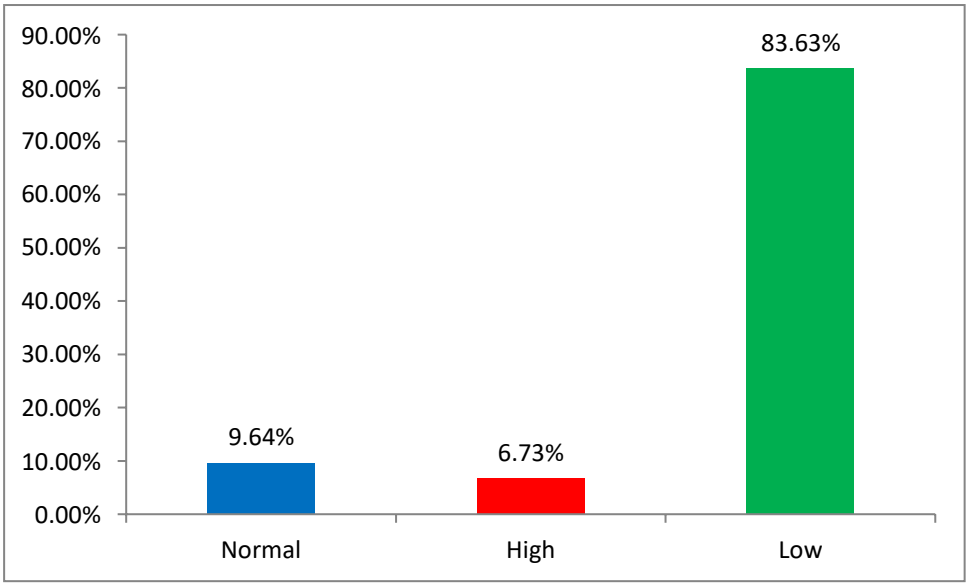

Figure 8: Distribution of patients by ACE marker analysis

3.2.3. Metastasis and Tumor Marker Levels:

In our study, 89.19% of patients who developed metastases exhibited elevated CA15-3 levels. Similarly, elevated CEA levels were found in 32.96% of cases with metastases (Figures 9 and 10).

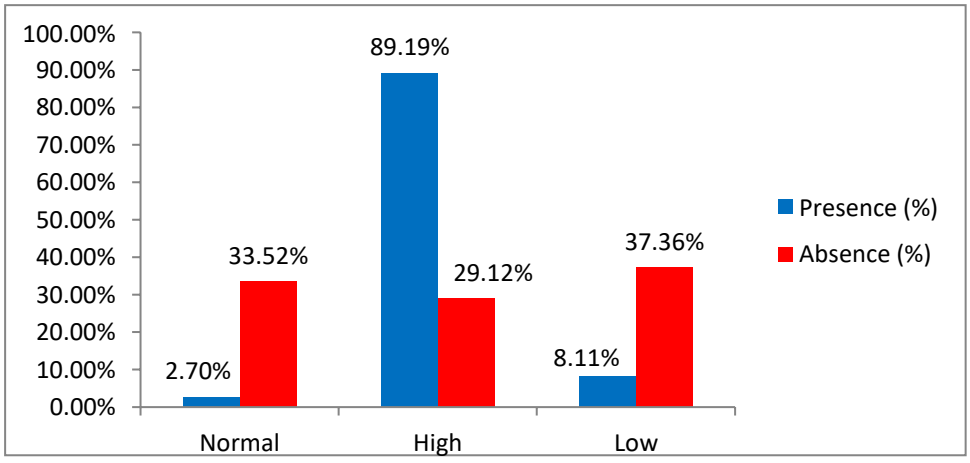

Figure 9: Distribution of patients by metastasis development and CA15-3 tumor marker levels

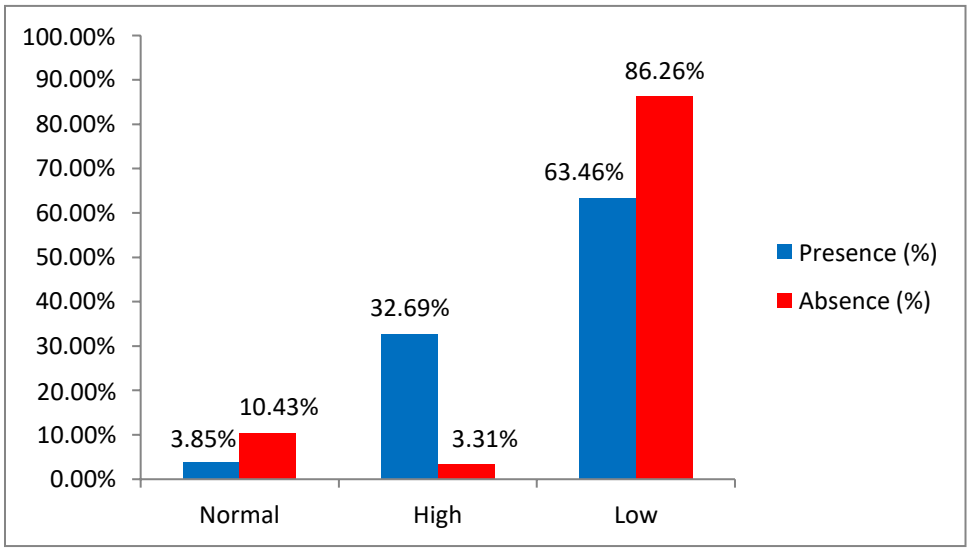

Figure 10: Distribution of patients by metastasis development and ACE tumor marker

II. Discussion

The objective of our study was to conduct a retrospective analysis to examine the clinical aspects of breast cancer and evaluate the significance of tumor markers, particularly CA15-3, in managing these patients. We recorded 470 cases, including 13 men and 457 women with breast cancer.

Regarding cancer localization, our findings show that the right and left breasts are almost equally affected. However, other studies have reported a predominance of left breast involvement (Diallo et al., 1996).

Histologically, carcinoma was the most common type (88.3% of cases), followed by sarcoma (11.7%). These results are consistent with studies from Senegal and Vietnam (Nguyen et al., 2017). The majority of cases were classified as Stage I or II, unlike the study by Jung (2015), which reported a predominance of Stage III (59.6%).

Regarding SBR grades, Grade II tumors were the most frequent (46.4%), followed by Grades III and I, which is consistent with the study by Hamdi et al. (2017). However, a Tunisian study by Sahraoui et al. (2017) showed a predominance of Grade III tumors (41% of cases).

For molecular subtypes, HER2+ was the most frequent (57.4%) in our study, followed by luminal B (19.25%), luminal A (17.01%), and TNBC (9.34%). These results differ from the literature, which generally reports that luminal A and B subtypes are the most frequent (Puig-Vives et al., 2008; Clarke et al., 2012).

In our study, only 11.5% of patients had developed metastases. These findings are in disagreement with Moroccan (Mechita, 2016) and Chinese (Wu, 2017) studies, which found lower metastasis rates of 63.6% and 48.5%, respectively (Mechita et al., 2016; Wu et al., 2017). A statistically significant relationship was found in our research between the development of metastases and elevated levels of these markers ($p = 0.0001$). According to the literature, the more advanced the stage, the higher the tumor marker levels (Giai M et al., 1996; O'Hanlon et al., 1995). Pre-therapeutic levels of CA15-3 and CEA, extremely elevated (5 to 10 times the normal values), increase with the progression of the disease and may indicate advanced or metastatic disease from the outset (Hayes et al., 1986).

However, these observations differ from those of Yasasever (1994), who analyzed the usefulness of various markers (CA15-3 and CEA) in detecting early metastases in untreated primary breast cancer patients. According to his multivariate analysis, no marker reliably distinguished the presence or absence of initial metastases (Yasasever et al., 1994).

Furthermore, to evaluate the response to metastasis treatment, our results confirm that the two tumor markers, CA15-3 and CEA, can be used to monitor tumor activity in the breast during treatment stages, as well as to assess how the body is responding to the treatment. Indeed, CA15-3 helps predict recurrence approximately 5 to 6 months before the appearance of symptoms and signs (Siaka, 2021).

Conclusion

Tumor markers, particularly CA15-3 and CEA, play a key role in diagnosis, recurrence prevention, and treatment monitoring, thus contributing to the optimal management of breast cancer patients.

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