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Profile of CA 15-3 and CEA during breast cancer chemotherapy at Ouagadougou, Burkina Faso

Fabienne Marie SOUDRE[1,2*], Alice KIBA[1,3], Arnaud KOURAOGO[1,4], Raoul KARFO[1,4], Aboubacar BAMBARA[1,6], Arsène KAGAMBEGA[6], Elie KABRE[1,5] and Jean SAKANDE[1,4]

[1]Unit of Training and Research in Health Sciences, University Joseph Ki-Zerbo, 03 P. O. Box 7021, Ouagadougou, Burkina Faso.
[2]Pediatric University Hospital Centre, Charles de Gaulle, 01 P. O. Box 1198, Ouagadougou, Burkina Faso.
[3]University Hospital Centre of Tengandogo, 11 P. O. Box 104, Ouagadougou, Burkina Faso.
[4]University Hospital Centre of Yalgado, Ouédraogo, 01 P. O. Box 5234, Ouagadougou, Burkina Faso.
[5]Public Health National Laboratory, 09 P. O. Box 24, Ouagadougou, Burkina Faso.
[6]University Hospital Centre of Bogodogo, 14 P. O. Box 371, Ouagadougou, Burkina Faso.

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Biomarkers are considered as an innovative tool in the diagnosis and follow-up of breast cancer. The aim of the study was to assess the profile of circulating tumour markers CA 15-3 and CEA in patients under chemotherapy for breast cancer in Ouagadougou. This is a prospective cross-sectional study with a descriptive and analytical aims which was done from July to November 2020. Patients with histologically confirmed malignant breast tumour and under chemotherapy were included. Results revealed that the study was on thirty (30) female patients whose average age was 47.47 ± 2.10 years with a mean BMI of 27.29 ± 1.09 kg/m^2. It was a non-specific type of infiltrating carcinoma with SBRm II grade in 90% of the patients. The mean CA 15-3 was 212.98 U/mL before chemotherapy and 165.75 U/mL after it. The CEA mean value was 3.13 ng/L before chemotherapy and 16.14 ng/L after it. Serum CA 15-3 was significantly associated with tumour site, SBRm grade, chemotherapy line and treatment response. Serum CEA level was significantly associated with tumour site and SBRm grade. Despite their lack of sensitivity, tumour markers, particularly CA 15-3 enabled assessment of the response to treatment in patients in this study.

Key words: Tumour markers, CA 15-3, CEA, breast cancer, chemotherapy.

INTRODUCTION

In Burkina Faso, breast cancer is responsible for 17.7% of cancer-related deaths in women. The treatment of this cancer is multidisciplinary and is often based on a strategy combining chemotherapy, surgery, radiotherapy, hormone therapy and/or targeted therapy. In Burkina Faso, chemotherapy plays an important role and is an

*Corresponding author. E-mail: fabysoudre@gmail.com Tel: +226 70 45 51 06.

integral part of care of patients suffering from all types of cancer. It constitutes an important component of effective care for breast cancer: given to patients at an early stage, it has a good impact on survival and contributes to cure. However, once treatment fails, patients' quality of life and survival rate are significantly affected. Therefore, it is essential to identify reliable prognostic factors to guide decision-making during the treatment of breast cancer in order to improve prognosis. This is how treatment has made great strides over the past decades with the discovery of prognostic biomarkers which make possible the use of individualized treatments. The concentration of circulating marker detected in the biological fluid is an indirect estimator of tumour mass or tumour aggressiveness; thus, allowing the assessment of tumour progression and/or therapeutic efficacy (Uygur and Gümüş, 2021).

Of all serum tumour markers for breast cancer, CA 15-3 and CEA were most used and recommended (Ashour Byomy et al., 2021; Imran et al., 2021; Khushk et al., 2021; Uygur and Gümüş, 2021). The European Group on Tumour Markers recommended that CEA and CA15-3 levels should be used for prognosis assessment, early detection of disease progression and monitoring of breast cancer treatment (Cardoso et al., 2019). While some authors suggested routine testing of tumour markers, the systematic use of serum markers in the strategies of women follow-up after breast cancer treatment is excluded from international main guidelines (Moschetti et al., 2016).

With these controversies in the monitoring of breast cancer patients, we therefore wanted to focus on the measurement of CA 15-3 and CEA in patients with a malignant breast tumour and treated by chemotherapy at Ouagadougou (Burkina Faso), with the aim of contributing to an early detection of metastases and/or therapeutic failure.

MATERIALS AND METHODS

Study context, type and period

This was a prospective cross-sectional study with descriptive and analytical aims led from July to November 2020. Patients were recruited at the University Hospital Centre of Bogodogo and at Sandof Polyclinic in Ouagadougou, Burkina Faso. Serum marker assays were performed in the laboratory of Sandof Polyclinic.

Samples

The tests were performed on the patients' serum, after venous blood sampling on dry tube. For the pre-therapeutic assays, samples were taken before the first course of chemotherapy. The results of these pre-therapy assays were extracted from the patients' files.

For the post-therapy samples, we took the samples at the end of the patients' last chemotherapy treatment (six-treatment protocols). The samples were centrifuged at 3500 rpm for 5 min, then the serum was aliquoted and stored at -80°C until analysis (Farahani et al., 2020).

Approach

Sampling was comprehensive during the period of study. Patients were selected in collection centres after file study among patients under chemotherapy for breast cancer and meeting the following criteria: histologically confirmed breast malignancy; patients with at least four courses of treatment allowing assessment of chemotherapy efficiency; complete clinical record; being aged at least 18 years and have given their free and informed consent to participate in the study. Patients had to be undergoing adjuvant or neoadjuvant chemotherapy to be included in the study and those undergoing palliative chemotherapy were not included. Patients who were not clinically and/or radiologically assessed for progression on chemotherapy were not also included.

Socio-demographic characteristics were obtained by interviewing the patients. Clinical and histological data were obtained from patients' records, consultation and hospitalization registers. Evaluation of hormone receptor status, HER2 expression and quantification of the Ki67 proliferation index were performed by immunohistochemical techniques, and the results were extracted from the patients' files. The immunohistochemical study was performed on paraffin sections by manual technique, using the Ultravision Quanto detection system kit, with DAB (Shi et al., 1999).

CA 15-3 and CEA Serum concentrations were determined in patients' serum using VIDAS® CA 15-3 (153) kit, reference 30429-01 and VIDAS® CEA(S) (CEAS) kit, reference 30 453-01, on the Biomérieux® Minividas automated system by ELFA technic (Enzyme Linked Fluorescent Assay) (Deliu et al., 2018; Abed et al., 2020). The normal serum values retained for CA15-3 and CEA were respectively < 30 U/mL and < 5 ng/mL.

For the study, clinical tumour response and imaging response (RECIST (Dubreuil et al., 2017) assessed by the oncologists and available in the patients' files were used and compared with the results of tumour marker assays.

Tumour response was considered as good in patients with complete or partial remission and poor when the patient was in stabilization or progression.

All study data were entered in Excel and analyzed using Stata version 13.0 software. Student T test was used to compare the averages between the different groups. Statistical tests were considered significant when p was less than 0.05.

The study was approved by the institutional Ethics Committee of Saint Camille CERBA (Pietro Annigoni Biomolecular Research Centre), reference N° 2020/II-03-016. Authorisation for data collection was obtained from the management of each collection centre. Data confidentiality was maintained throughout the study.

RESULTS

A total of thirty (30) patients were included in the study; ten (10) patients at the University Hospital Centre of Bogodogo and twenty (20) at Sandof Polyclinic.

Socio-demographic characteristics

The mean age of the patients in the study was 47.47 ± 2.10 years; with extremes ranging from 33 to 74 years. 16 patients (53.33%) were under 45 years old and 14 (46.67%) were over 45 years old. The average body mass index (BMI) was 27.29 ± 1.09 kg/m^2 (ranging from 13.76 to 39.67 kg/m^2). Of the patients, 11 (36.67%) had a normal BMI, while 19 (63.33%) were overweight or obese. Two patients (6.67%) had a personal history of

Table 1. Distribution of patients according to clinical and histological characteristics.

Parameter	Characteristics	Number (n=30)	%
Location of tumour	Right breast	18	60.00
	Left breast	10	33.33
	Bilateral	2	6.67
Location on breast (n=21)	QSE	18	60.00
	Other locations	12	40.00
Tumour size (T)	T2	7	23.33
	T3	1	3.33
	T4	13	43.34
	Tx	9	30.00
Number of lymphadenopathy (N)	N0	3	10.00
	N1	17	56.67
	N2/N3	2	6.66
	Nx	8	26.67
Metastases (M)	M0	19	63.33
	M1	11	36.67
SBRm	II	27	90.00
	III	3	10.00
Histological type	NSIC*	27	90.00
	DCIN**	2	6.67
	ILC***	1	3.33

* Non-specific infiltrating carcinoma **Ductal carcinoma in situ ***Infiltrating lobular carcinoma.

breast cancer and four (13.33%) had a family history of breast cancer.

Clinical and histological characteristics

Tumour damage was predominant on the right breast of 18 patients (60%). Tumour mass was present in the upper-external quadrant in 60.00% of patients and the histological grade SBRm II was the most found (90%). The majority of women were on their first line chemotherapy (70%) and metastases were present in 36.67%, mainly bone metastases.

The distribution of patients according to clinical and histological characteristics is presented in Table 1.

Immunohistochemical characteristics

In the population studied, 13 patients (43.33%) were able to perform hormone receptor (ER and PR) evaluation: 11 (84.62%) were positive and 2 (15.38%) were negative. Moreover, 10 patients (33.33%) were tested for HER2 protein and Ki67 antigen. All HER2 results were negative; four patients (40%) had Ki67 ≤ 25% and six (60%) had Ki67 > 25%. Thus, we got 84.62% luminal A tumours and 15.38% triple negative tumours.

Chemotherapeutic characteristics

The majority of patients (70%; that is 21 patients) were on first-line chemotherapy, while nine (9) patients (30%) were at least on second-line chemotherapy. The main protocol used was FAC (5 Fluorouracil, Adriblastine, Cyclophosphamide) administered to 56.67% of patients. Fourteen (14) patients (46.67%) had a satisfactory response to chemotherapy assessed by clinical and/or imaging studies, while sixteen (16) (53.33%) had a poor response.

Circulating tumour markers

CA 15-3 was measured in 12 patients (40%) before the start of chemotherapy, while CEA was available in 7

Table 2. Pre- and post-treatment concentrations of tumour markers.

Tumour marker		Average	Standard deviation	p-value	Minimum	Maximum
CA 15-3 (U/mL)	Pre-therapeutic (n=12)	212.98	180.28		8.30	2194.21
	Post-therapeutic (n=12)	137.69	57.11	0.677	13.75	570.84
	Post-therapeutic (n=30)	165.75	76.50	0.136	9.30	2273.32
CEA (ng/L)	Pre-therapeutic (n=7)	3.13	0.38		2.19	4.87
	Post-therapeutic (n=7)	5.31	4.04	0.597	1.62	29.48
	Post-therapeutic (n=30)	16.14	10.90	0.357	0.66	324.43

Table 3. Post-therapeutic changes of CA 15-3 and CEA according to the epidemiological characteristics of patients.

Parameter	Characteristics	CA 15-3		CEA	
		Mean U/mL	p-value	Mean ng/L	p-value
Age	≤ 45 years (n=16)	44.76±09.02	0.091	1.59±0.39	0.157
	> 45 years (n=14)	304.04±158.46		32.77±22.97	
BMI	Normal (n=11)	172.78±50.20	0.946	11.23±6.35	0.738
	High (n=19)	161.69±118.63		18.99±16.97	
PH* of breast cancer	Yes (n=2)	38.08±13.44	0.663	1.03±0.11	0.718
	No (n=28)	174.87±81.78		17.22±11.66	
FH** of breast cancer	Yes (n=4)	23.11±5.89	0.474	3.78±2.23	0.664
	No (n=26)	187.70±87.68		18.04±12.56	

PH*: personal history FH**: family history.

patients (23.33%). The mean concentrations of tumour markers drawn from the patients' records (pre-therapeutic CA 15-3 and CEA) and those obtained from our assays (post-therapeutic CA 15-3 and CEA) are shown in Table 2. Subsequently, the mean CA 15-3 and CEA values before chemotherapy were 212.98±180.28 U/mL and 3.13±0.38 ng/L respectively. Of the 12 patients with pre-therapy CA 15-3, five had high values and seven had normal values. For the pre-therapeutic CEA, all seven patients had normal values. After chemotherapy, the mean CA 15-3 was 165.75±76.50 U/mL and the CEA was 16.14±10.90 ng/l.

Study of the variation of post-therapeutic CA 15-3 and CEA according to patients' characteristics

Tables 3, 4 and 5 summarize post-treatment variations of CA 15-3 and CEA respectively according to the epidemiological, clinical and histological, immune-histochemical and chemotherapeutic characteristics of the patients. Thus, the markers showed statistically significant variations depending on the site of the tumour, the presence of metastases, SBRm grade, chemotherapy line and response to treatment.

DISCUSSION

The objective of the study was to assess the profile of circulating markers CA 15-3 and CEA in patients under chemotherapy for breast cancer at Ouagadougou. The main limitation of the study is the size of the sample obtained, which does not allow the conclusions to be extrapolated to the entire population of patients treated for breast cancer. Only 40 and 23.33% of the patients had respectively benefited from CA15-3 and CEA tests before treatment. Although these biomarkers are not recommended for cancer screening, diagnosis or staging (Harris et al., 2007), the interest of pre-therapeutic initial values is clearly established, especially for a comparison with later figures. Indeed, the interest of measuring their levels before any treatment is to have an individual reference value which is essential to assess the effectiveness of a treatment and/or to carry out a later monitoring. The detection of a biological recurrence is

Table 4. Post-therapeutic changes of CA 15-3 and CEA according to clinical and histological features.

Parameter	Characteristics	CA 15-3		CEA	
		Mean U/mL	p-value	Mean ng/L	p-value
Location of tumour	Unilateral (n=28) Bilateral (n=2)	85.56±24.41 1288.50±984.82	0.000	5.60±2.58 163.73±160.69	0.000
Location on breast	QSE (n=18) Others (n=12)	220.50±125.62 83.63±31.07	0.390	23.61±18.07 4.93±2.59	0.411
Tumour size (T)	T2/T3 (n=8) T4/Tx (n=22)	173.75±74.92 162.85±101.68	0.951	14.44±8.51 16.76±14.66	0.927
Number of lymphadenopathy (N)	N0/Nx (n=11) N1/N2/N3 (n=19)	47.19±26.46 234.40±118.10	0.245	4.33±2.86 22.98±17.10	0.419
Metastases (M)	M0 (n=19) M1 (n=11)	53.97±18.07 358.83±198.45	0.026	2.45±0.56 39.79±29.16	0.099
SBRm	II (n=27) III (n=3)	98.82±26.24 768.15±752.59	0.003	5.83±2.67 108.97±107.73	0.001
Histological type	NSIC (n=27) Others (n=3)	182.88±84.50 11.62±1.20	0.511	17.80±12.09 1.26±0.28	0.657

Table 5. Post-therapeutic changes of CA 15-3 and CEA according to chemotherapeutic immunohistochemical characteristics.

Parameter	Characteristics	CA 15-3		CEA	
		Mean U/mL	p-value	Mean ng/L	p-value
Hormone receptors	Yes (n=13) No (n=17)	277.16±172.55 80.56±24.41	0.208	34.65±24.74 1.99±0.40	0.140
Immunohistochemical classification	Luminal A (n=11) Triple negative (n=2)	320.29±202.51 39.96±11.55	0.580	40.68±29.06 1.50±0.58	0.590
Ki67	≤ 25 % (n=4) > 25 % (n=6)	724.87±531.79 107.56±50.75	0.185	98.86±76.79 8.74±5.01	0.178
Chemotherapy line	1st line (n=21) Multiple lines (n=9)	68.28±20.65 393.20±242.87	0.024	3.63±1.55 45.33±35.63	0.079
Response to chemotherapy	Good (n=14) Poor (n=16)	24.51±3.77 289.35±137.92	0.042	1.67±0.44 28.80±20.19	0.220

earlier if one refers to the basal value of each patient rather than to a single statistical threshold (Yoo et al., 2021).

The mean pre-therapeutic CA 15-3 was 212.98 U/mL (Table 2), well above the normal value (<30 U/mL). On the other hand, the mean pre-therapeutic CEA was 3.13 ng/L (Table 2); all patients had a normal value < 5 ng/L. The clinical significance of preoperative serum levels of CEA and CA 15-3 in breast cancer remains controversial. Indeed, Molina et al. (2010) found abnormal serum levels of CEA (> 5 µg / L) or CA 15.3 (> 30 kU / L) respectively in 12.7 and 19.6% of their patients. Serum concentrations of CEA and CA 15-3 were clearly linked to tumour size and lymph node damage, with significantly higher

concentrations in large size tumours and those with lymph node damage (Molina et al., 2010). The lack of sensitivity and specificity of CEA led the expert groups to not recommend its measurement in the screening and diagnosis of carcinomas of various locations. Even in the initial assessment, the value of its measurement remains debated at the international level and some experts do not recommend it because it does not modify the therapeutic attitude (Durand and Beaudeux, 2011).

Post-therapy CA 15-3 and CEA values were 137.69 U/mL (n=12) and 5.31 ng/L (n=7), respectively, a decrease in the mean value for the former marker and an increase for the latter, but not statistically significant (Table 2). Of the patients with normal CA 15-3 before chemotherapy, five (5) maintained values below 30 U/mL, as did CEA, which remained normal. These pre-therapeutic markers allowed us to infer a good prognosis which was confirmed by the clinical course of the patients. Many authors highlighted the correlation between the evolving profile of CA 15-3 and the response to treatment, and various recommendations stipulate that an initial elevation of CA 15-3 which does not return to the normal reflects a lack of response to treatment and constitutes an important unfavourable prognosis factor (Bushi and Trebicka, 2021). No significant variation of tumour markers was found based on epidemiological characteristics in the study (Table 3). However, analysis of marker variations based on clinical and histological characteristics revealed a significant association with tumour site and SBRm grade for both markers; and with presence of metastases for CA 15-3 (Table 4). We did not find a significant association of CA 15-3 and CEA values with the immunohistochemical characteristics of the patients (Table 5). Li et al. (2018) did not also find any difference of serum marker levels based on immunohistochemistry. On the contrary, other studies showed that CA15-3 levels differ significantly according to molecular subtype (Li et al., 2020; Ruswendro et al., 2021).

Variations of CA 15-3 were statistically significant according to patients' treatment line and response to chemotherapy; whereas the mean values of CEA showed no statistically significant variation according to these characteristics (Table V). Indeed, patients with a poor response to chemotherapy, as well as those who were at least at their second line had higher CA 15-3 values (Table V). The pattern was similar for CEA even if the variations were not statistically significant (Table 5). Then, CA 15-3 values were clearly linked with prognosis in patients and predicted response to treatment in our patients. The prognostic value of CA15-3 had been proven by some studies (Gonssaud et al., 2017; Li et al., 2018; Uygur and Gümüş, 2021), while other studies reported negative results (Rasmy et al., 2016). For Ebeling et al. (2002) in a study of 1046 patients, CA15-3 in univariate analysis but not in multivariate analysis was predictive of a poor outcome. In a review paper, Duffy (2006) collected at least 10 studies and reported in a descriptive way that higher CA15-3 may be associated with a poor outcome, but he did not perform a pooled analysis to confirm the results. The reason why CA15-3 can predict breast cancer prognosis is not very clear, but as CA15-3 is the soluble form of MUC1, this may be related to the function of MUC1. It has been reported that MUC1 does not only allow cancer cells to escape the immune system, but also promotes cancer cell migration by activating certain membrane receptors (Oral et al., 2020; Khodabakhsh et al., 2021). CEA is less widely studied as a prognostic factor than CA15-3 because it is less positive and more controversial. Some studies reported that CEA does not allow to distinguish primary from metastatic breast cancer (Ebeling et al., 2002; Molina et al., 2010; Nan et al., 2017), but others reported that high CEA levels were associated with a poor prognosis of breast cancer (Li et al., 2018; Imran et al., 2021; Ashour Byomy et al., 2021). These conflicting results of CA15-3 and CEA in breast cancer with respect to their prognostic value may be due to small sample sizes, variable study designs or other biases in each study. At present, the use of serum tumour markers in breast cancer is poorly established due to their low sensitivity and specificity. Many studies reported low positive CA15-3 and even lower CEA (Shao et al., 2015; Wu et al., 2014). Without more potent serum markers, although imperfect, CA15-3 and CEA remain the most commonly used biomarkers in breast cancer and are recommended for practical use by the American Society of Clinical Oncology (ASCO) (Harris et al., 2007). Likewise, the European Group on Tumour Markers recommended the use of CA15-3 and CEA to assess the prognosis of breast cancer (Duffy et al., 2017).

Conclusion

As the most common malignancy in women, breast cancer is a great threat for women's health worldwide. Its treatment by chemotherapy requires relevant clinical, radiological and biological evidence to assess the response to treatment. Our study allowed a quantitative assessment of tumour markers CA 15-3 and CEA. The main limitations of the study are the size of the population and the fact that tumour markers were measured in a limited number of patients before chemotherapy. Our results suggest that the levels of these markers, particularly CA 15-3, may be useful in predicting the prognosis of breast cancer in patients. As the examination of these markers is still not widely used in daily clinical practice, the data obtained provided important information for identifying patients with a poor response to chemotherapy. However, individual biological monitoring should be ensured by a single laboratory and a single technique. Interpretation of the levels of these markers must take into account their evolutionary

profiles, but also the clinical and radiological conditions of the patients.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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REFERENCES

Abed SN, Mahdi HS, Sahib AS, Mousa HM, Almaali A, Al Haydar M, Mohsin KK (2020). Serum Levels of Cancer Antigen 15.3 and Estrogen in a Samples of Iraqi Women with Breast Cancer Treated with Anastrazole. International Journal of Pharmaceutical Research 1:1604-1608.

Ashour Byomy LG, Zahraan F, Aref M, Ibrahim Mosa MF (2021). Assessment of CEA and CA15-3 as Potential Prognostic Markers for Breast Cancer in Egyptian Females. Alfarama Journal of Basic and Applied Sciences 2(1):44-50.

Bushi S, Trebicka A (2021). The Role of Tumor Markers for Evaluation the Course of Chemotherapy. ARC Journal of Cancer Science 7(1):01-05.

Cardoso F, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, Rubio IT, Zackrisson S, Senkus E (2019). Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†. Annals of Oncology 30(8):1194-1220.

Deliu I, Cristina M, Dumitru G (2018). Utility of tumor markers as a diagnostic tool. Current Trends in Natural Sciences 7(14) :272-275.

Dubreuil J, Cachin F, Berriolo-Ridinger A, Skanjeti A (2017). Critères d'interprétation en imagerie cancérologique solide: RECIST, PERCIST…. Médecine Nucléaire 41(3):241-248.

Duffy MJ (2006). Serum Tumor Markers in Breast Cancer: Are They of Clinical Value? Clinical Chemistry 52(3):345-351.

Duffy MJ, Harbeck N, Nap M, Molina R, Nicolini A, Senkus E, Cardoso F (2017). Clinical use of biomarkers in breast cancer: Updated guidelines from the European Group on Tumor Markers (EGTM). European Journal of Cancer 75:284-298.

Durand G, Beaudeux JL (2011). Biochimie médicale: Marqueurs actuels et perspectives. Lavoisier.

Ebeling FG, Stieber P. Untch M, Nagel D, Konecny GE, Schmitt UM, Fateh-Moghadam A, Seidel D (2002). Serum CEA and CA 15-3 as prognostic factors in primary breast cancer. British Journal of Cancer, 86(8):1217-1222.

Farahani H, Amri J, Alaee M, Mohaghegh F, Rafiee M (2020). Serum and Saliva Levels of Cancer Antigen 15-3, Carcinoembryonic Antigen, Estradiol, Vaspin, and Obestatin as Biomarkers for the Diagnosis of Breast Cancer in Postmenopausal Women. Laboratory Medicine 51(6):620-627.

Gonssaud B, Goussot V, Berriolo-Riedinger A, Saïtta-Aribau E, Coutant C, Cochet A, Fumoleau P, Riedinger,JM (2017). Clinical value of CA 15-3 for detection of distant metastases in newly diagnosed breast cancer. Annales De Biologie Clinique 75(4):421-429.

Harris L, Fritsche H, Mennel R, Norton L, Ravdin P, Taube S, Somerfield MR, Hayes DF, Bast Jr. RC (2007). American Society of Clinical Oncology 2007 update of recommendations for the use of tumor markers in breast cancer. Journal of Clinical Oncology 25(33):5287-5312.

Imran AH, Al-atrachji SA, Al-mosawi KK (2021). Clinical important of E-Cadherin, CA15-3 and CEA in Diagnostic and Flow Up for Breast Cancer Patients. Indian Journal of Forensic Medicine and Toxicology 15(2).

Khodabakhsh F, Merikhian P, Eisavand MR, Farahmand L (2021). Crosstalk between MUC1 and VEGF in angiogenesis and metastasis: A review highlighting roles of the MUC1 with an emphasis on metastatic and angiogenic signaling. Cancer Cell International 21(1):1-11.

Khushk M, Khan A, Rehman A, Sheraz S, Tunio YM, Rehman K, Rehman D, Ahmed M, Abbas K, Khan ME (2021). The Role of Tumor Markers: Carcinoembryonic Antigen and Cancer Antigen 15-3 in Patients With Breast Cancer. Cureus 13(7).

Li J, Liu L, Feng Z, Wang X, Huang Y, Dai H, Zhang L, Song F, Wang D, Zhang P, Ma B, Li H, Zheng H, Song F, Chen K (2020). Tumor markers CA15-3, CA125, CEA and breast cancer survival by molecular subtype: A cohort study. Breast Cancer (Tokyo, Japan), 27(4).

Li X, Dai D, Chen B, Tang H, Xie X, Wei W (2018). Clinicopathological and Prognostic Significance of Cancer Antigen 15-3 and Carcinoembryonic Antigen in Breast Cancer: A Meta-Analysis including 12,993 Patients. Disease Markers.

Molina R, Auge JM, Farrus B, Zanón G, Pahisa J, Muñoz M, Torne A, Filella X, Escudero JM, Fernandez P, Velasco M (2010). Prospective Evaluation of Carcinoembryonic Antigen (CEA) and Carbohydrate Antigen 15.3 (CA 15.3) in Patients with Primary Locoregional Breast Cancer. Clinical Chemistry 56(7):1148-1157.

Moschetti I, Cinquini M, Lambertini M, Levaggi A, Liberati A (2016). Follow-up strategies for women treated for early breast cancer. Cochrane Database of Systematic Reviews 5.

Nan J, Li J, Li X, Guo G, Wen X, Tian Y (2017). Preoperative Serum Carcinoembryonic Antigen as a Marker for Predicting the Outcome of Three Cancers. Biomarkers in Cancer 9, 1179299X17690142.

Oral O, Unverdi H, Kumcu E, Turkbey D, Dogan S, Hucumenoglu S (2020). Associations between the expression of mucins (MUC1, MUC2, MUC5AC and MUC6) and clinicopathologic parameters of human breast carcinomas. Indian Journal of Pathology and Microbiology 63(4):551-558.

Rasmy A, Abozeed W, Elsamany S, Baiomy ME, Nashwa A, Amrallah A, Hasaan E, Alzahrani A, Faris M, Alsaleh K, AlFaraj A (2016). Correlation of Preoperative Ki67 and Serum CA15.3 Levels with Outcome in Early Breast Cancers a Multi Institutional Study. Asian Pacific Journal of Cancer Prevention 17(7):3595-3600.

Ruswendro D, Syamsu SA, Thabry R, Seweng A, Usman AN (2021). Association between molecular subtype of local advanced breast cancer with Ca 15-3 level. Breast Disease 40(s1):S119-S122.

Shao Y, Sun X, He Y, Liu C, Liu H (2015). Elevated Levels of Serum Tumor Markers CEA and CA15-3 Are Prognostic Parameters for Different Molecular Subtypes of Breast Cancer. PLOS ONE 10(7):e0133830.

Shi SR, Guo J, Cote RJ, Young L, Hawes D, Shi Y, Thu S, Taylor CR (1999). Applied Immunohistochemistry and Molecular Morphology 7(3):201.

Uygur MM, Gümüş M (2021). The utility of serum tumor markers CEA and CA 15–3 for breast cancer prognosis and their association with clinicopathological parameters. Cancer Treatment and Research Communications 28:100402.

Wu S, He Z, Zhou J, Sun J, Li F, Lin Q, Guo L, Lin H (2014). Serum levels of CEA and CA15-3 in different molecular subtypes and prognostic value in Chinese breast cancer. Breast (Edinburgh, Scotland) 23(1):88-93.

Yoo YC, Park S, Kim HJ, Jung HE, Kim JY, Kim MH (2021). Preoperative Routine Laboratory Markers for Predicting Postoperative Recurrence and Death in Patients with Breast Cancer. Journal of Clinical Medicine 10(12):2610.