Clinicopathological, Treatment and Event-Free Survival Characteristics in a Moroccan Population of Triple-Negative Breast Cancer

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ABSTRACT

INTRODUCTION: Triple-negative breast cancer (TNBC) is a group of breast carcinoma characterized by the lack of expression of estrogen and progesterone hormone receptors (ER, PgR) and HER2. This form is also characterized by its aggressiveness, a low survival rate, and the absence of targeted therapies. This study was planned to evaluate the clinical features, treatment, and prognosis characteristics of TNBC in a population of Moroccan patients.

METHODS: In this retrospective study, a total of 905 patients diagnosed with breast cancer at the National Institute of Oncology in Rabat, Morocco, have been included. Based on molecular subtype, patients were divided into 2 categories: TNBC and non-TNBC patients. Data were recorded from patients’ medical files and analyzed using SPSS 13.0 software (IBM).

RESULTS: Overall, 17% of the patients had TNBC. At diagnosis, the median age of TNBC cases was 47 years, with extreme ages of 40 and 55 years. The median follow-up time was 30 months (10-53 months) and the 3-year survival rate was 76%. No significant difference was observed among the patients in terms of age at diagnosis, age at menarche, age at the time of first birth, nulliparity, oral contraception, and family history of breast cancer. Menopausal status and the number of pregnancy were significantly higher in the non-TNBC group. The percentage of grade 3 (G3) tumors was higher in the TNBC group (P<.001). Using neoadjuvant, adjuvant chemotherapy and radiotherapy, a net benefit in the event-free survival was registered for the 2 groups.

CONCLUSIONS: This retrospective study was very informative and showed that women with TNBC had a less favorable prognosis than non-TNBC cases. Clinical data demonstrated that risk factors including age, premenopausal status, parity, hormonal contraceptive use, advanced disease, and a high histologic grade were independently associated with TNBC. However, large tumors and high Scarff-Bloom and Richardson grade prevail in TNBC cases with a higher incidence of lymph node metastases.

KEYWORDS: Breast cancer, triple-negative, non-triple-negative, risk factors, event-free survival, molecular subtypes

Introduction

Worldwide, breast cancer (BC) is the most prevalent and the first leading cause of cancer death among females. Breast cancer represents 24.2% of all cancers in women and about 11.6% of all new cancer cases.1 In 2018, the World Health Organization (WHO) has estimated that more than 630000 women died due to BC.1

Triple-negative breast cancer (TNBC) is an aggressive tumor form accounting for approximately 15% to 20% of all BC cases.2 This subtype is defined pathologically by the absence of expression of the estrogen receptor (ER) and progesterone receptor (PgR) and does not exhibit amplification of the human epidermal growth factor receptor 2 gene (HER2).1

Triple-negative breast cancer is a highly heterogeneous form of BC. This subtype is characterized by diagnosis at a younger age, larger tumor size, high-tumor grade, high mitotic index, and higher rate of mortality.4,5 Moreover, it is widely reported that TNBC constitutes an aggressive BC subtype because it is usually associated with a high frequency of metastasis with distinct metastatic patterns and a relatively high recurrence rate and it is usually accompanied by a significant decrease in overall survival (OAS).6 Patients with TNBC are more likely to experience relapse within the first 3 years and are at high risk of death in the first 5 years following diagnosis.7

In Morocco, data from different oncology centers converge toward its characterization as an aggressive form that occurs at a young age and poses a real health problem.2,10 This retrospective study was planned to investigate epidemiological and clinicopathological characteristics, treatment outcome, and survival rate in a Moroccan population with TNBC and to compare them with non-TNBC cases.
Methods

Study design and population

This retrospective study was conducted in the National Institute of Oncology in Rabat, Morocco. A total of 905 BC cases diagnosed in 2009 and followed up until 2014 were included in the study. For each patient, the medical record was carefully reviewed to obtain information regarding clinical, pathological, and therapeutic characteristics. A total of 405 cases with missed data, foreign people, and men patients were excluded and the remaining 500 BC cases were divided according to their molecular subtype into 2 groups: 85 patients with TNBC in group 1 (G1) and 415 non-TNBC patients in group 2 (G2).

The study was conducted concerning legal aspects and was approved by the Ethical Committee of Biological Research, Faculty of Medicine and Pharmacy—Rabat.

Data collection

Data were recorded from patients’ medical files. The medical records were retrospectively reviewed and information regarding age, anthropometry measurement (weight and height), familial history of BC, hormonal status, clinical data, cancer stage, tumor size, histological type, tumor grade, lymph node involvement, metastases, hormonal receptors, treatment (surgery, chemotherapy, radiation therapy, hormonal therapy), and follow-up was collected using SPSS software.

The histological type was recorded and updated according to the latest WHO classification of breast tumors. Pathological tumor-node-metastasis (pTNM) staging was done according to the TNM classification of the seventh edition of the American Joint Committee on Cancer (AJCC) classification. Histological tumor grading was evaluated according to Scarff-Bloom and Richardson (SBR) grading system modified by Singletary et al., and vascular invasion was quantified histologically.

Immunohistochemical analysis was used to determine ER and PgR status and was performed using standard procedures on 4-μm sections of paraffin-embedded tissue specimens stained with the monoclonal antibodies 6F11 and 1A6, respectively. Accordingly, ER and PgR were considered positive when the nuclear expression was observed in at least 10% of the tumor cells.

Immunohistochemical expression of Her2 was evaluated according to cytoplasmic membrane staining of the infiltrative component, concerning the intensity and the percentage of stained cells and taking into account the complete or incomplete membrane staining. Results are expressed in scores: 0/1+ for negative, 2+ for ambiguous, and 3+ for positive staining. Fluorescent in situ hybridization (FISH) was performed to assess Her2 amplification when the score was ambiguous. Accordingly, if the Her2 amplification is confirmed by FISH, the case was considered HER2 positive.

Follow-up

Patients were followed up until December 2014. Event-free survival (EFS) was calculated from the date of surgery or the date of starting the first course of chemotherapy to the date of loco-regional recurrence or distant metastasis.

Statistical analysis

Statistical analysis was performed using SPSS software version 13.0 (IBM, Armonk, NY, USA). Descriptive variables were expressed as mean ± SD or median (interquartile range). Differences between qualitative data were assessed using the chi-square test. Survival rate calculation was performed by the Kaplan-Meier method and compared using the log-rank test.

Univariate and multivariate Cox regression model was performed to compare variables and outcomes. The difference is considered significant if the P value is <.05. In the multivariate model, all parameters reported in previous studies to influence survival rates were included even if these parameters were not significant in the univariate model of this study.

Results

Clinicopathological characteristics

Concerning inclusion/exclusion criteria, 17% of BC cases registered at the National Institute of Oncology in Rabat have a TNBC (85/500). Clinical and pathological data are reported, respectively, in Tables 1 and 2.

A complete database is given as an online supplementary file. Overall, the median age at diagnosis of TNBC cases was 47 ± 11.75, with extreme ages at 40 and 55 years. Only 14.9% of the cases have a familial history of BC. In this study, TNBC and non-TNBC cases shared the same distribution regarding clinical data.

A comparison between TNBC and non-TNBC cases showed a statistically significant difference for the number of full-term pregnancies (P = .003) and menopausal status (P = .035). A total of 41.4% of TNBC cases have more than 4 children as compared with non-TNBC cases. Moreover, 51.4% of TNBC cases (37/72) and only 37.8% of non-TNBC cases (122/323) are menopausal. The other parameters, including age, age at menarche, nulliparity at diagnosis, oral contraception use, and anthropometric data, did not show statistically significant differences between TNBC and non-TNBC cases.

The pathological characteristics of TNBC cases clearly show the predominance of N0 lymph node status and SBR grade III.

Comparison between TNBC and non-TNBC cases showed significant differences regarding intraductal components (P = .001), SBR grade (P = .001), and vascular invasion (P = .033).
Table 1. Comparative clinical data.

| VARIABLES                        | ALL PATIENTS, % | TNBC, % | NON-TNBC, % | P VALUE |
|----------------------------------|-----------------|---------|-------------|---------|
| Nulliparity at diagnosis         |                 |         |             |         |
| Yes                              | 89 (22.7)       | 14 (20.0) | 75 (23.3)  | .638    |
| No                               | 303 (77.3)      | 56 (80.0) | 247 (76.7) |         |
| Number of cases with full-term pregnancies |                 |         |             |         |
| 0                                | 89 (22.6)       | 14 (20.0) | 75 (23.2)  | .003    |
| 1                                | 43 (10.9)       | 14 (20.0) | 29 (9.0)   |         |
| 2-4                              | 131 (33.3)      | 13 (18.6) | 118 (36.5) |         |
| >5                               | 130 (33.1)      | 29 (41.4) | 101 (31.3) |         |
| Oral contraception use           |                 |         |             |         |
| Yes                              | 127 (42.2)      | 25 (50.0) | 102 (40.6) | .272    |
| No                               | 174 (57.8)      | 25 (50.0) | 149 (59.4) |         |
| Menopausal status                |                 |         |             |         |
| Yes                              | 159 (40.3)      | 37 (51.4) | 122 (37.8) | .035    |
| No                               | 236 (59.7)      | 35 (48.6) | 201 (62.2) |         |
| Familial history of BC           |                 |         |             |         |
| Yes                              | 54 (14.7)       | 10 (14.9) | 44 (14.7)  | 1.000   |
| No                               | 313 (85.3)      | 57 (85.1) | 256 (85.3) |         |
| Clinical signs                   |                 |         |             |         |
| Yes                              | 45 (10.5)       | 10 (13.2) | 35 (10.0)  | —       |
| No                               | 382 (89.5)      | 66 (86.8) | 316 (90.0) |         |
| Age                              |                 |         |             |         |
| <50                              | 249 (58.6)      | 41 (54.7) | 208 (59.4) | .519    |
| ≥50                              | 176 (41.4)      | 34 (45.3) | 142 (40.6) |         |
| Age at menarche                  |                 |         |             |         |
| <12                              | 33 (33)         | 4 (28.6)  | 29 (33.7)  | .873    |
| 13-14                            | 43 (43)         | 6 (42.9)  | 37 (43.0)  |         |
| ≥15                              | 24 (24)         | 4 (28.6)  | 20 (23.3)  |         |
| Breast side                      |                 |         |             |         |
| Right                            | 209 (49.2)      | 33 (44.0) | 176 (50.3) | .373    |
| Left                             | 216 (50.8)      | 42 (56.0) | 174 (49.7) |         |
| Body mass index                  |                 |         |             |         |
| Thinness                         | 6 (2.2)         | 1 (1.9)  | 5 (2.3)    | .056    |
| Normal weight                    | 90 (33.1)       | 10 (18.9) | 80 (36.5)  |         |
| Overweight                       | 99 (36.4)       | 26 (49.1) | 73 (33.3)  |         |
| Obesity                          | 77 (28.3)       | 16 (30.2) | 61 (27.9)  |         |

Abbreviation: TNBC, triple-negative breast cancer.
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Patients with TNBC and non-TNBC received the same treatments as no specific treatment is recommended for TNBC cases; hormonal and Herceptin treatments are exclusively given to patients with positive hormone and Her2 receptors. Comparative treatment data between TNBC and non-TNBC cases are summarized in Table 3. Statistical analysis did not show any significant difference for the 4 treatment modalities.

Analysis of EFS

The estimated median follow-up period was 30 ± 21.28 (10-53) months with extreme ranges of 3 to 67 months. Event-free survival was calculated using univariate analysis by Kaplan-Meier method and results are reported in Figure 1. The 3-year EFS of patients with the local disease was 76% and 83% of women with TNBC and non-TNBC, respectively. After 5 years, the EFS was higher in patients with TNBC (73%) than in patients with non-TNBC (65%). The difference between EFS in TNBC and non-TNBC patients is not statistically significant (P = .42). Results of EFS correlation to some relevant parameters are represented in Figures 2 and 3. Event-free survival is poorer in TNBC women with N3 lymph nodes (P = .00).

In non-TNBC women, EFS is better in patients with N3 lymph nodes (P = .00).

Univariate and multivariate Cox regression analysis

The results of univariate and multivariate Cox regression analyses are reported in Table 4. Univariate analysis indicated that N3 lymph node, chemotherapy, and radiotherapy are statistically significant parameters influencing EFS in women with TNBC. Univariate analysis showed that, among non-TNBC cases, inflammatory BC, N2 and N3 status, presence of vascular invasion, radiotherapy, chemotherapy, and hormone therapy are associated with poorer EFS.

Concerning N3 lymph node status, the risk of relapse is higher in the TNBC group (18.46; P = .001) as compared with the non-TNBC group (5.19; P = .001). Of particular interest, the administration of neoadjuvant chemotherapy is a risk factor for both TNBC group (10.12; 0.00-34.14; P = .001) and non-TNBC group (3.10, 1.66-5.81; P = .001). However, adjuvant chemotherapy was beneficial for progression-free survival. In fact, the relapse risk was lower, corresponding to 0.17 (P = .005) for patients with TNBC and 0.32 (P = .001) for non-TNBC

Table 2. Comparative pathological data by TNBC groups.

| VARIABLES           | ALL PATIENTS, % | TNBC, % | NON-TNBC, % | P VALUE |
|---------------------|-----------------|---------|-------------|---------|
| Tumor size          |                 |         |             |         |
| T1                  | 88 (23.2)       | 11 (18.3) | 77 (24.1)   | .154    |
| T2                  | 207 (54.5)      | 30 (50.0) | 177 (55.3)  |         |
| T3                  | 85 (22.4)       | 19 (31.7) | 66 (20.6)   |         |
| Lymph nodes         |                 |         |             |         |
| N0                  | 153 (39.8)      | 30 (51.7) | 123 (37.7)  | .164    |
| N1                  | 109 (28.4)      | 16 (27.6) | 93 (28.5)   |         |
| N2                  | 65 (16.9)       | 6 (10.3)  | 59 (18.1)   |         |
| N3                  | 57 (14.8)       | 6 (10.3)  | 51 (15.6)   |         |
| Intraductal components |               |         |             |         |
| Yes                 | 183 (52.6)      | 17 (30.9) | 166 (56.7)  | .001    |
| No                  | 165 (47.4)      | 38 (69.1) | 127 (43.3)  |         |
| Vascular invasion   |                 |         |             |         |
| Yes                 | 151 (39.8)      | 17 (27.4) | 134 (42.3)  | .033    |
| No                  | 228 (60.2)      | 45 (72.6) | 183 (57.7)  |         |
| SBR grade           |                 |         |             |         |
| SBR I               | 29 (7.3)        | 3 (4.6)  | 26 (7.8)    | .001    |
| SBR II              | 230 (57.8)      | 26 (40.0) | 204 (61.3)  |         |
| SBR III             | 139 (34)        | 36 (55.4) | 103 (30.9)  |         |

Abbreviations: N, nodes; SBR, Scarff-Bloom and Richardson classification; TNBC, triple-negative breast cancer.
patients. For radiotherapy, the risk of relapse was lower for both TNBC and non-TNBC patients, with 0.024 (P = .001) and 0.38 (P = .001), respectively. For non-TNBC group, the risk of relapse after hormone therapy was 0.20 (P = .001).

Multivariate analysis showed no statistically significant results for TNBC cases. However, in non-TNBC cases, the multivariate analysis highlighted the same results than the univariate analysis regarding N3 status, presence of vascular invasion, radiotherapy, and hormone therapy.

**Discussion**

Worldwide, epidemiological and clinical data clearly showed that TNBC is an aggressive form of BC and is associated with a poor prognosis and a low EFS rising on a great challenge in the global management of BC. In Morocco, limited data on TNBC are available and studies were conducted on small size series.\(^7\)^\(^8\)^\(^10\) Therefore, this study was planned to be a large one to assess the epidemiology profile, tumor characteristics, and treatment patterns of TNBC cases compared with non-TNBC cases recruited in the National Institute of Oncology (INO) in Rabat. National Institute of Oncology is considered as the reference public health oncology center in Morocco and receives patients from the whole country.

In this study, TNBC was reported in 17% of BC cases, which is comparable to previously reported data in Morocco.\(^7\)^\(^8\)^\(^10\) Table 5 reports the prevalence of TNBC in Morocco as compared with other North African countries and some sub-Saharan, European, American, and Asian countries.

Triple-negative breast cancer prevalence in Morocco is in agreement with obtained data in the other North African countries (Algeria and Tunisia) and much lower than almost sub-Saharan countries. These results highlight the high prevalence of TNBC in sub-Saharan countries that could be due to some genetic factors or attributed to some technical limitations leading to an overestimation of false-positive/negative results in performing and interoperating immunohistochemistry analysis related to ER, PR, and Her2 expression.

**Figure 1.** Event-free survival (EFS) in TNBC/non-TNBC patients with local disease. TNBC indicates triple-negative breast cancer.

**Table 3.** Comparative treatment data by TNBC groups.

| VARIABLES                  | ALL PATIENTS, % | TNBC, % | NON-TNBC, % | P VALUE |
|---------------------------|-----------------|---------|-------------|---------|
| Neoadjuvant chemotherapy  |                 |         |             |         |
| Yes                       | 76 (19.1)       | 20 (26.3) | 56 (17.4)  | .104    |
| No                        | 321 (80.9)      | 56 (73.7) | 265 (82.6) |         |
| Adjuvant chemotherapy     |                 |         |             |         |
| Yes                       | 322 (79.1)      | 55 (76.4) | 267 (79.7) | .632    |
| No                        | 85 (20.9)       | 17 (23.6) | 68 (20.3)  |         |
| Radiotherapy              |                 |         |             |         |
| Yes                       | 276 (64.8)      | 50 (65.8) | 226 (64.6) | .895    |
| No                        | 150 (35.2)      | 26 (34.2) | 124 (35.4) |         |
| Surgery                   |                 |         |             |         |
| Tumorectomy               | 95 (23.5)       | 20 (29.4) | 75 (22.3)  | .213    |
| Mastectomy                | 309 (76.5)      | 48 (70.6) | 261 (77.7) |         |
| Hormone therapy           |                 |         |             |         |
| Yes                       | —               | —       | 273 (65.8) | —       |
| No                        | —               | —       | 142 (34.2) |         |

Abbreviation: TNBC, triple-negative breast cancer.
studies reported by Plasilova et al, showing that the risk for developing TNBC rises with increasing parity and increasing the waist-to-hip ratio circumference, suggesting a complex interaction of genetic biomarkers and societal factors.

Triple-negative breast cancer and patients’ age are well studied and discussed. Some results showed that in all ethnic/racial groups, the incidence of TNBC increased among young patients. In the United States, Plasilova et al have reported that in white patients, TNBC prevails in patients below age 40, whereas in black patients, the incidence of TNBC is still higher until age 60. Of particular interest, the age of BC onset is 10 years earlier than in Western countries. This finding is in...
Table 4. Univariate and multivariate Cox regression analysis for event-free survival (EFS).

| VARIABLES       | TNBC                      |                        | NON-TNBC                      |                        |
|-----------------|----------------------------|------------------------|-------------------------------|------------------------|
|                 | UNIVARIATE ANALYSIS        | MULTIVARIATE ANALYSIS  | UNIVARIATE ANALYSIS           | MULTIVARIATE ANALYSIS  |
|                 | HR | 95% CI | P VALUE | HR | 95% CI | P VALUE | HR | 95% CI | P VALUE | HR | 95% CI | P VALUE |
| Nulliparity     | No | 1      | 1       | Yes | 1.54 | 0.32-7.84 | 0.59 | 0.16 | 0.00-> | 0.94 | 1.20 | 0.63-2.28 | 0.57 |
| OC use          | No | 1      | 1       | Yes | 0.01 | 0.00-6.23 | 0.17 | 0.01 | 0.00-> | 0.61 | 1.01 | 0.51-2.00 | 0.95 |
| FHBC            | No | 1      | 1       | Yes | 2.01 | 0.41-9.76 | 0.38 | 19.55 | 0.00-> | 0.90 | 1.01 | 0.43-2.40 | 0.96 |
| Obesity         | No | 1      | 1       | Yes | 0.02 | 0.00-6.86 | 0.19 | 143  | 0.00-> | 0.98 | 1.23 | 0.61-2.45 | 0.55 |
| IBC             | No | 1      | 1       | Yes | 2.43 | 0.52-11.28 | 0.25 | 2.66 | 1.24-5.70 | 0.01 | 0.65 | 1.19-2.26 | 0.50 |
| Tumor size, mm  | <20 | 1      | 1       | 21-50 | >    | 0.00-> | 0.94 | 1.41 | 0.60-3.30 | 0.42 |
|                 | >   | 0.00-> | 0.94    | >   | 0.00-> | 0.94    | 2.25 | 0.89-5.72 | 0.08 |
| SBR grade       | I   | 1      | 1       | II  | >    | 0.00-> | 0.95 | 2.36 | 0.31-17.58 | 0.40 |
|                 | III | >    | 0.00-> | 0.96 | 5.97 | 0.80-44.16 | 0.80 |
| N status        | N0  | 1      | 1       | N1  | 0.9  | 0.08-10.14 | 0.94 | 5.87 | 0.00-> | 0.95 | 1.33 | 0.54-3.29 | 0.52 |
|                 |     | 1      | 1       |     | 1.29 | 0.47-3.49 | 0.61 |

(Continued)
| VARIABLES                  | TNBC UNIVARIATE ANALYSIS | TNBC MULTIVARIATE ANALYSIS | NON-TNBC UNIVARIATE ANALYSIS | NON-TNBC MULTIVARIATE ANALYSIS |
|---------------------------|--------------------------|----------------------------|----------------------------|-------------------------------|
|                           | HR  | 95% CI       | P VALUE         | HR  | 95% CI       | P VALUE         | HR  | 95% CI       | P VALUE         | HR  | 95% CI       | P VALUE         |
|                           |     |              |                 |     |              |                 |     |              |                 |     |              |                 |
| N2                        | 2.41| 0.21-26.72   | 0.47            | 0.65| 0.00-0.99    | 0.99            | 3.34| 1.38-8.09    | 0.00            | 2.43| 0.89-6.63    | 0.08            |
| N3                        | 18.46| 2.76-123.26 | 0.00            | 1.54| 0.00-0.99    | 0.99            | 5.19| 2.29-11.76   | 0.00            | 3.71| 1.35-10.21   | 0.01            |
| LVI                       | No  | 1            | 1               | Yes | 3.54| 0.94-13.26  | 0.06            | 28.86| 0.00-0.99   | 0.90            | 1.83| 1.01-3.32   | 0.04            |
|                           | Yes | 3.54| 0.94-13.26  | 0.06            | 28.86| 0.00-0.99   | 0.90            | 1.83| 1.01-3.32   | 0.04            | 1.12| 1.07-4.20   | 0.03            |
| Surgery type              |     |              |                 |     |              |                 |     |              |                 |     |              |                 |
|                           |     |              |                 |     |              |                 |     |              |                 |     |              |                 |
| Radical mastectomy        | No  | 1            | 1               | Yes | 0.02| 0.00-1.13   | 0.00            | 0.00| 0.00-0.99   | 0.91            | 0.38| 0.22-0.68   | 0.00            |
|                           | Yes | 0.02| 0.00-1.13   | 0.00            | 0.00| 0.00-0.99   | 0.91            | 0.38| 0.22-0.68   | 0.00            | 0.44| 0.21-0.93   | 0.03            |
| Radiotherapy              |     |              |                 |     |              |                 |     |              |                 |     |              |                 |
|                           |     |              |                 |     |              |                 |     |              |                 |     |              |                 |
| Neoadjuvant chemotherapy  | No  | 1            | 1               | Yes | 10.12| 3.00-34.14 | 0.00            | 30.11| 0.00-0.99   | 0.89            | 3.10| 1.66-5.81   | 0.00            |
|                           | Yes | 10.12| 3.00-34.14 | 0.00            | 30.11| 0.00-0.99   | 0.89            | 3.10| 1.66-5.81   | 0.00            | 1.76| 0.51-6.09   | 1.76            |
| Adjuvant chemotherapy     |     |              |                 |     |              |                 |     |              |                 |     |              |                 |
|                           |     |              |                 |     |              |                 |     |              |                 |     |              |                 |
| Trastuzumab               | No  | —            | —               | Yes | 0.17| 0.05-0.59   | 0.00            | 93.55| 0.00-0.99   | 0.90            | 0.32| 0.17-0.59   | 0.00            |
|                           | Yes | —            | —               | 0.17| 0.05-0.59   | 0.00            | 93.55| 0.00-0.99   | 0.90            | 0.32| 0.17-0.59   | 0.00            |
| Hormone therapy           |     |              |                 |     |              |                 |     |              |                 |     |              |                 |
|                           |     |              |                 |     |              |                 |     |              |                 |     |              |                 |
| Abbreviations: CI, confidence interval; FHBC, family history of breast cancer; HR, hazard ratio; iBC, inflammatory breast cancer; SBR, Scarff-Bloom and Richardson classification; TNBC, triple-negative breast cancer.
agreement with previous studies in patients with TNBC from Tunisia. A recent study conducted in Morocco highlighted the high frequency of BC in young women as compared with Western countries. In this study, both TNBC and non-TNBC cases prevail in younger women, with no statistical difference between the 2 groups.

Worldwide, published data show that TNBC cases are characterized by bigger tumor sizes and high-grade histology. Regarding tumor size, there is no statistical difference between TNBC and non-TNBC groups in this study. Of particular interest, Dent et al have conducted a long-term follow-up of 1608 patients with BC and found that the recurrence of TNBC did not correlate with the tumor size.

The association between lymph node status and TNBC is controversial. Some authors report that lymph node negativity is more frequent in TNBC. Others support a higher frequency of lymph node positivity and this lymph node positivity is associated with a poor prognosis, whereas some publications suggest the absence of any association between increased tumor diameter and lymph node metastasis. In this study, most of the TNBC cases exhibit an SBR grade III as compared with non-TNBC cases (55.4% vs 30.9%). Large tumors and high SBR grade are in favor of a high lymph node metastases incidence. However, after adjustment of these factors, the incidence of positive nodes with TNBC is considerably less than non-TNBC, which is in agreement with previously reported data. Conversely, some other studies show that there is no statistical correlation of lymph nodes status between TNBC and non-TNBC groups.

Table 5. Comparison of TNBC frequencies.

| REGION OF THE WORLD | FREQUENCY OF TNBC, % | COUNTRY | STUDY         |
|---------------------|----------------------|---------|---------------|
| Maghreb (North Africa) | 17                   | Morocco | This Study    |
|                     | 22.5                 | Tunisia | Fourati et al |
|                     | 19.77                | Algeria | Gaceb et al  |
| Sub-Saharan Africa  | 18                   | Tunisia | Der et al    |
|                     | 82                   | Ghana   | Der et al    |
|                     | 46                   | Mali    | Ly et al     |
|                     | 36                   | Kenya   | Der et al    |
|                     | 32                   | Uganda  | Der et al    |
|                     | 27                   | Kenya   | Der et al    |
|                     | 23                   | Kenya   | Der et al    |
|                     | 15.9                 | Sudan   | Der et al    |
| Europe              | 11                   | Italy   | Minicozzi et al |
| USA                 | 23.7                 | African Americans | Plasilova et al |
| Asia                | 29.8                 | India   | Der et al    |
|                     | 25                   | India   | Der et al    |
|                     | 21                   | Indonesia | Der et al    |
|                     | 17.6                 | Malaysia | Der et al    |
|                     | 15                   | Malaysia | Der et al    |
|                     | 12.9                 | Chinese | Su et al     |
|                     | 8.9                  | Philippines | Plasilova et al |

Abbreviation: TNBC, triple-negative breast cancer.
This study is very informative highlighting the main characteristics of TNBC cases in our population. The main limitations of the study are as follows: (1) the absence of a date of death in the medical records, which limited the calculation of the OAS, and (2) the noncomplete data in some patients’ files that could have influenced the analysis.

Conclusions

Understanding the pathogenesis of TNBC and molecular and immunological characteristics of the disease is the key for better management of this heterogeneous disease. Clinical data highlighted that TNBC have the worse outcome compared with the non-TNBC. Moreover, common risk factors including age, premenopausal status, increased parity, hormonal contraceptive use, high histologic grade, and advanced disease were independently associated with TNBC.

Nowadays, many promising therapeutic pathways are investigated, but without a comprehensive consideration of TNBC pathogenesis, predicting the effectiveness of these strategies will be compromised.

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Author Contributions

FZM participated in the project design, data collection, and statistical analysis and drafted the manuscript. MS participated in data collection and statistical analysis. RR was in charge of the statistical analysis and drafted the manuscript. MS participated in the project design, data collection, and statistical analysis.

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Supplemental material

Supplemental material for this article is available online.

REFERENCES

1. GLOBOCAN. Estimated incidence, mortality and prevalence worldwide in 2018. https://gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf. Updated 2018.
2. Spugnese L, Gabriele M, Scarpati R, et al. Germline mutations in DNA repair genes may predict neoadjuvant therapy response in triple-negative breast patients. Genes Chromosomes Cancer. 2016;55:915-924.
3. Palma G, Frasci G, Chiariello A, et al. Triple-negative breast cancer: looking for the missing link between biology and treatments. OncoTargets. 2015;6:26560-26574.
4. Carey LA, Perou CM, Livasy CA, et al. Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. JAMA. 2006;295:2492-2502.
5. Sturza LA, Mihely J, Manulla K, Shriver CD, Ellsworth RE. Outcome disparities in African American women with triple-negative breast cancer: a comparison of epidemiological and molecular factors between African American and Caucasian women with triple-negative breast cancer. BMC Cancer. 2014;14:62.

6. Kanani YM, Sampey BP, Beyene D, et al. Metabolic profile of triple-negative breast cancer in African-American women reveals potential biomarkers of aggressive disease. Cancer Genomics Proteomics. 2014;11:279-294.
7. Derkouati T, Bakkach J, Mansouri M, et al. Triple-negative breast cancer in North of Morocco: clinicopathologic and prognostic features. BMC Women Health. 2016;16:668.
8. Akashi Y, Bennis S, Abbas F, et al. Clinicopathological, therapeutic and prognostic features of the triple-negative tumors in Moroccan breast cancer patients (experience of Hassan II university hospital in Fez). BMC Res Notes. 2011;4:500.
9. Al Jarroudi O, Abda N, Brahim S, Alqir S. Triple negative breast cancer at the University Hospital Mohammed VI-Oujda. Asian Pac J Cancer Prev. 2017;18:195-200.
10. Rais G, Raisouis S, Aitelah M, et al. Triple-negative breast cancer in Moroccan women: clinicopathological and therapeutic study at the National Institute of Oncology. BMC Womens Health. 2012;12:35.
11. Simpleray SE, Alred CF, Ashley P, et al. Revision of the American Joint Committee on Cancer staging system for breast cancer. J Clin Oncol. 2002;20:3628-3636.
12. Derkaoui T, Bakkach J, Mansouri M, et al. Triple-negative breast cancer in North of Morocco: clinicopathologic and therapeutic study at the National Institute of Oncology.(experience of Hassan II university hospital in Fez). BMC Res Notes. 2011;4:500.
13. Singletary SE, Alred CF, Ashley P, et al. Revision of the American Joint Committee on Cancer staging system for breast cancer. J Clin Oncol. 2002;20:3628-3636.
14. Fourati A, Boussen H, El May MV, et al. Descriptive analysis of molecular subtypes in Tunisian breast cancer. Asia Pac J Clin Oncol. 2014;10:e69-74.
15. Gaceh H, Cherbal F, Bakkour R, Ould Ronia A, Mahfoud H. Clinicopathological and molecular study of triple-negative breast cancer in Algerian patients. Pathol Oncol Res. 2018;24:297-308.
16. Der EM, Gvasi RK, Tetter Y, et al. Triple-negative breast cancer in Ghanaian women: the Korle Bu Teaching Hospital experience. Breast. 2015;21:627-633.
17. Ly M, Antoine M, Dembele AK, et al. High incidence of triple-negative tumors in sub-Saharan Africa: a prospective study of breast cancer characteristics and risk factors in Malian women seen in a Bamako University Hospital. Oncology. 2012;83:257-263.
18. Minicorzi P, Bella F, Toss A, et al. Relative and disease-free survival for breast cancer in relation to subtype: a population-based study. J Clin Oncol Res. 2013;13:15-90-1577.
19. Piasilova ML, Hayse B, Killelea BK, Horowitz NR, Chaggar AB, Lannin DR. Features of triple-negative breast cancer: analysis of 38,813 cases from the national cancer database. Medscape. 2016;95:60464.
20. Su Y, Zheng Y, Zheng W, et al. Distinct distribution and prognostic significance of multiple molecular subtypes of breast cancer in Chinese women: a population-based cohort study. BMC Cancer. 2011;11:292.
21. Bauer KR, Brown M, Cress RD, Parise CA, Caggiano V. Descriptive analysis of estrogen receptor (ER)-negative, progesterone receptor (PR)-negative, and HER2-negative invasive breast cancer, the so-called triple-negative phenotype. Cancer. 2007;109:1721-1728.
22. Parise CA, Bauer KR, Caggiano V. Variation in breast cancer subtypes with age and race/ethnicity. Crit Rev Oncol Hematol. 2010;76:44-52.
23. Shaouri M, Mouh FZ, Ghannam I, Razine R, El Mouh M, Amrou M. Outcome of breast cancer in Moroccan young women correlated to clinicopathological features, risk factors and treatment: a comparative study of 716 cases in a single institution. J PLA. 2016;11:0164841.
24. Qiu JDXX, Li R, Wang JD. Clinicopathological features and prognosis of triple-negative breast cancer: a comparison between younger (<60) and elderly (≥60) patients. Eur J Cancer Care. 2016;25:1065-1075.
25. Yamamoto Y, Iwase H. Clinicopathological features and treatment strategy for triple-negative breast cancer. Int J Clin Oncol. 2010;15:341-351.
26. Dent R, Trudeau M, Pritchard KI, et al. Triple-negative breast cancer: clinical features and patterns of recurrence. Clin Cancer Res. 2007;13:4429-4444.
27. Oakman C, Viale G, Di Leo A. Management of triple-negative breast cancer. Breast. 2010;19:312-321.
28. Rakha EA, Reis-Filho JS, Ellis IO. Basal-like breast cancer: a critical review. Clin Breast Cancer. 2008;8:256-2581.
29. Cabibi SJ, Cheang MC, Leung S, et al. Basal breast cancer molecular subtype predicts for lower incidence of axillary lymph node metastases in primary breast cancer. Clin Breast Cancer. 2008;8:249-256.
30. Sayed S, Moloo Z, Waikie R, et al. Is breast cancer from Sub Saharan Africa truly receptor poor? Prevalence of ER/PR/HER2 in breast cancer from Kenya. Breast. 2014;23:591-596.
31. Keegan TH, Press DJ, Tao L, et al. Impact of breast cancer subtypes on 3-year survival among adolescent and young adult women. Breast Cancer Res. 2013;15(5):R95.
32. Onitilo AA, Engel JM, Greenlee RT, Mukeh BN. Breast cancer subtypes based on ER/PR and HER2 expression: comparison of clinicopathologic features and survival. Clin Med Res. 2009;7(2-4):13.