New

The 1st and only registered chemotherapy after failure of a platinum-containing regimen in advanced or metastatic TCCU
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AMAAC Introduction
The Arab Medical Association Against Cancer (AMAAC) is a medical body that was established in 2001 as part of the Arab Medical Association where its main office is located in Cairo - Egypt, and it is also a continuation of the Arab Council Against Cancer that was founded in 1995. The Executive Committee of (AMAAC) is represented by two members who are named officially by the Oncology Society of each Arab Country.

The Arab Medical Association Against Cancer aims at strengthening relationships between members in different Arab Countries to raise the level of cooperation in the field of oncology on both scientific and practical aspects. Exchanging information and researches between members through Regional and Arab Conferences and Publications. Holding Public Awareness Campaigns in the field of oncology that are organized by Arab Countries. Participating in scientific activities with International Oncology Societies. Finally, encouraging researchers and doctors to meet and exchange experiences together with finding training opportunities in the field of oncology inside and outside the Arab World.

The officially nominated members of AMAAC by the Oncology Societies of each country

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First-line therapy with Docetaxel and Gemcitabine in chemotherapy naive metastatic breast cancer: A Phase II Study

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Key words: Breast cancer, gemcitabine, docetaxel, first-line, chemotherapy naïve.

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Abstract

Purpose: This phase II study of biweekly docetaxel and gemcitabine was performed to investigate the efficacy and safety of this combination in treatment of patients with metastatic breast cancer.

Patients and Methods: This study included 40 patients with previously untreated, stage IV breast cancer, the period between October 2008 and July 2011. Therapy consisted of 50 mg/m² of docetaxel and 1500 mg/m² gemcitabine, both administered on days 1 and 15 every 4 weeks.

Results: A total of 40 patients were evaluated by intention-to-treat analysis for efficacy and safety. The overall response rate (ORR) was 65% (complete and partial response, 10 and 55%, respectively). Non-hematological toxicity was more common than hematological toxicity, with alopecia and asthenia were the most frequently reported adverse events. Severe hematological toxicity was rare.

Conclusions: Biweekly docetaxel plus gemcitabine appears to be very effective and fairly well-tolerated regimen for the treatment of patients with metastatic breast cancer.

No authors report any conflict of interest.

A written informed consent was obtained from each patient in accordance with institutional and government guidelines.

Introduction

In most developed countries, breast cancer is second only to lung cancer as the most common cause of cancer-related death in women [1]; therefore, it represents a serious health-care problem. Systemic therapy for patients with metastatic breast cancer (MBC) consists of hormonal therapy and cytotoxic chemotherapy. Anthracyclines (doxorubicin and epirubicin) can yield response rates of around 20-40% in MBC patients when used as single agents, and up to 60% when combined with other cytotoxic drugs [2]. However, the efficacy achieved with anthracyclines comes at the cost of high toxicity. Recently, new cytotoxic drugs with high activity were emerged, such as taxanes (paclitaxel and docetaxel), vinorelbine, gemcitabine, and capecitabine. These drugs have raised the hopes of patients with MBC to experience higher efficacy with tolerable toxicity. Many studies showed that combination chemotherapy may be more effective than single-agent therapy [3, 4]. Development of new agents and/or drug combinations with a superior therapeutic index remains a principal goal of investigational efforts. Gemcitabine (difluorodeoxycytidine, dFdC) possesses a broad range of activity against various solid tumors including advanced breast cancer patients (ABC), and is characterized by a favorable toxicity profile [5]. Gemcitabine has a complex mechanism of action that may involve incorporation into replicating DNA and termination of DNA chain elongation. It also has a favorable safety profile, with myelosuppression, mild nausea and lethargy as its major toxicities [6]. Gemcitabine can be used as single agent or in combination regimens, it showed an objective response rate (ORR) of 25–46% in ABC patients, depending on whether this drug was used as first- or second-line treatment [7]. Docetaxel inhibits microtubule depolymerization with high percentage and more prolonged duration and causes cell cycle arrest in the radiosensitive G2-M phase [8]. And it aborts mitosis and causes cell death in the radioresistant S-phase, thereby exerting its cytotoxic effect at more than one point in the cell cycle [9]. The two drugs have distinct mechanisms of action and, with the exception of neutropenia, non-overlapping toxicities [6]. The combination of docetaxel with gemcitabine has been tested, both in chemonaive and pretreated patients [10]. In a study conducted by Ricotti and his co-workers found that both agents are active and it was seen that the sequence docetaxel-gemcitabine was characterized by a synergic effect, whereas the inverse sequence or simultaneous exposure to the two drugs induced an antagonistic effect. It was also observed that a 24-h exposure to docetaxel determined a cell cycle block in G2-M phase and that after 24 hours, the majority of cells had moved into G1-S, which is the most sensitive phase to the action of gemcitabine. Furthermore, the percentage of cells in apoptosis increased considerably after sequential docetaxel-gemcitabine treatment [11]. Based on the previously mentioned data we conducted the present study to evaluate the efficacy and toxicity of a regimen containing gemcitabine plus docetaxel in previously untreated patients with MBC. In order to minimize acute toxicities especially myelosuppression, we used a biweekly administration schedule.
Materials and Methods

Patient Population and Eligibility Criteria

Eligible patients had to be female, aged 18-70 years, and had histologic or cytologic diagnosis of breast carcinoma and stage IV disease. Prior chemotherapy was not allowed. Patients could not have received previous therapy with gemcitabine or a taxane. Other inclusion criteria included: World Health Organization (WHO) performance status ≤ 2, and estimated life expectancy of at least 12 weeks. Patients were required to have at least one bidimensionally measurable lesion. Prior radiation was permitted only if measurable disease was outside a previously irradiated area, if radiotherapy was not given to more than 50% of bone marrow volume, and if it was terminated at least 4 weeks prior to enrollment. Adequate hematological, renal and hepatic function was essential for all patients; where leucocytic count ≥4,000/mm3, platelet count ≥100,000/mm3, hemoglobin >9 g/dl, serum creatinine <1.4 mg/dl, serum bilirubin ≤1.5 mg/dl, serum transaminase ≤3×ULN in cases without liver metastases and ≤5×ULN in cases with liver metastases.

Exclusion criteria included:
active severe infection, severe heart disease, active concomitant malignancy (except in situ carcinoma of the cervix or adequately treated basal cell carcinoma of the skin), brain metastases, peripheral neuropathy and bone metastases as the only site of disease.

The study protocol was approved by the institution Ethics Committee and it conforms to the provisions of the Declaration of Helsinki (as revised in Seoul 2008).

Treatment plan

Forty patients with MBC received docetaxel 50 mg/m2 followed by gemcitabine 1500 mg/m2 both were given on days 1 and 15 to be repeated every 4 weeks. Chemotherapy Patients received docetaxel 50mg/m 2 diluted in 250 c.c normal saline 0.9% over 1hour intravenous (i.v) infusion on days 1 and 15, followed by gemcitabine 1500mg/m 2 diluted in 250c.c saline over 30 minutes i.v infusion on days 1 and 15. To avoid fluid retention and/or anaphylactic reactions, all patients must receive standard premedication with i.v. dexamethasone (20 mg), antihistamine, ranitidine Hcl (Zantac) and antiemetic treatment (ondansetron 16mg or granisetron 3mg) 1 hour before the start of therapy with docetaxel; dexamethasone must be taken the night before, morning of, and evening after treatment. Treatment was recycled every 4 weeks and to be continued in patients exhibiting a complete response (CR) or partial response (PR) for a maximum 8 cycles. Chemotherapy was stopped in case of progression, patient refusal and unacceptable toxicity. Patients who had received at least one cycle of chemotherapy were evaluated for toxicity and at least two cycles for efficacy. Granulocyte colony-stimulating factor (G-CSF) was used either curatively or as prophylaxis against febrile neutropenia.

Pre-treatment assessment and Post-treatment Reassessment

Each patient must have the following assessment tests before being enrolled into the study:
Full medical history and clinical examination, baseline tests included a full blood count, serum biochemistry (urea, creatinine and electrolytes, liver function tests, calcium). Staging procedure for all patients included CT scan of the chest and pelvisabdomen with contrast. CT scan and/or MRI of brain or a bone scan were also done. Patients were followed every 2 cycles of chemotherapy to document response (regression, stable disease or progression). Patients were followed after completion of the course of treatment monthly until disease progression or death. Radiological responses were documented by a CT scan and/or MRI. Treatment toxicity was classified according to the criteria of the World Health Organization (WHO) [12]. Tumor response was evaluated every two cycles of chemotherapy using the same evaluation method and it was classified according to the WHO criteria. A complete response (CR) was defined as the disappearance of any evidence of tumors for at least 4 weeks. A partial response (PR) was defined as ≥ 50% reduction in the sum of the products of the greatest perpendicular diameters of all lesions for at least 4 weeks. Stable disease (SD) was defined as <50% reduction or <25% increase in the products of the greatest perpendicular diameters of all lesions without any evidence of new lesions. Progressive disease (PD) was defined as an increase of ≥25% or the appearance of new lesions.

Dose adjustments for toxicity

Dose adjustments during treatment were made based on Absolute Neutrophil Count (ANC) and platelet counts performed within 24 hours prior to the start of therapy and clinical assessment of nonhematologic toxicities. The day-1 dose of each subsequent cycle depended on the toxicity seen in the previous cycle. The treatment was delayed until the ANC returned to 1500 and the platelet count to 100,000. Otherwise, full doses of both drugs were given, except in patients with WHO grade 4 neutropenia lasting >1 week, grade 4 neutropenia associated with fever ≥38.5°C, or grade 4 thrombocytopenia. In these circumstances, after recovery, the day 1 and 15 doses of both drugs were given at 75% of the dose given on day 1 of the last cycle. The observed nonhematologic toxicities (except alopecia and vomiting) had to return to WHO grade 0 to 1, or baseline conditions before resuming injections of both drugs. Doses in subsequent cycles were reduced to 75% or held for any grade 3 nonhematologic toxicity (except alopecia and vomiting) and, were reduced to 50% or held for any grade 4 nonhematologic toxicity. Patients were withdrawn from the study after 3 weeks of treatment delay due to any toxicity. If serum bilirubin was increased to >1.5 ×ULN or AST/ALT increased to >3 ×ULN in patients without liver metastasis and >5.0 ×ULN in patients with liver metastasis at the start of the next cycle then the cycle could not begin until serum bilirubin returned to ≤1.5 ×ULN and AST/ALT returned to ≤3 ×ULN in patients without liver metastasis and ≤5.0 ×ULN in patients with liver metastasis. If the values did not return to these limits within 42 days from Day 1 of the current cycle then the patient was discontinued from the study. The doses of gemcitabine and docetaxel were reduced by 20% in the subsequent cycle(s) if serum bilirubin was increased 2-folds or AST/ALT was increased 5-folds relative to baseline at any time during the cycle. Dose adjustments on Day 15 for hepatic toxicity had no effect on dosing in subsequent cycles. In the case of grade 2 arthralgia and/or myalgia, asthenia, or fatigue, the gemcitabine and docetaxel doses were reduced by 20% in all subsequent cycles. Treatment was discontinued if these toxicities were of grade 4.

Data analysis

Descriptive statistics were used to characterize study subjects and response to treatment. The primary end point of the study was the response rate. The toxicity was the secondary end point which was assessed as mentioned above using the (WHO criteria).Survival curves were established with the Kaplan-Meier method [13]. Overall survival was calculated from the date of starting treatment to the date of death or last follow-up; while Time to Tumor Progression (TTP) was calculated from the date of starting treatment to the date of evidence of progression, disease progression, or last contact. The data were analyzed with Graphpad prism software version 4.03.
**Results**

**Patient Characteristics**

Forty patients with MBC were enrolled in the study from October 2008 to July 2011 in Ain Shams University Hospitals and other private centers. A summary of the patient characteristics is shown in Table 1. Median age was 54 years (range 31–72). Hepatic and pulmonary metastases were present in a large proportion of patients (56%). All patients were eligible and assessable for response and toxicity.

<table>
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<tr>
<th>Characteristics</th>
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<td>Overexpressed</td>
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**Response**

A total of 204 cycles of chemotherapy were given for the patients in this study, with a median of 5 cycles per patient. Complete response occurred in 4(10%) patients; while partial response occurred in 22(55%) patients. Therefore, overall objective response rate was recorded in 26(65%) patients [95% confidence interval (CI) 56% - 80%]. Stable disease occurred in 8(20%) patients. Progressive disease occurred in 6(15%) patients (Table 2).

<table>
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<td>Complete response(CR)</td>
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<tr>
<td>Partial response(PR)</td>
<td>26(65%), 8(20%)</td>
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<tr>
<td>Overall response(ORR)</td>
<td>6(15%)</td>
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<tr>
<td>Stable disease(SD)</td>
<td>8(20%)</td>
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<tr>
<td>Progressive disease(PD)</td>
<td>2(5%)</td>
</tr>
</tbody>
</table>

After a median follow up time of 14.8 months (range 4-33 months), the median overall survival time was 14 months (95% CI, 4.5-17 months). While median Time to Tumor Progression (TTP) was 7 months (95% CI, 4.7-10 months) for patients who achieved initial response (CR, PR and SD). (Figures 1 and 2). The most common sites of disease progression were liver and lung, which were the most commonly involved sites at baseline.

**Toxicity**

Toxicity was assessed in 40 patients (Table 3). Asthenia was the most common grade 3/4 non-hematological toxicity which occurred in 8 (20%) patients, followed by nail disorders which occurred in 7 (18%) patients. Only 1 (2.5%) patient developed grade 3/4 anemia, and 2 (5%) patients developed grade 3/4 neutropenia, however, no febrile neutropenia was observed. No treatment related deaths (neither due to sepsis nor bleeding) were reported in the study.

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>grade 1/2</th>
<th>grade 3/4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Leucopenia</td>
<td>20</td>
<td>50</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>20</td>
<td>50</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>I- Hematological</td>
<td>40</td>
<td>100</td>
</tr>
<tr>
<td>Alopecia</td>
<td>24</td>
<td>60</td>
</tr>
<tr>
<td>Asthenia</td>
<td>10</td>
<td>25</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>20</td>
<td>50</td>
</tr>
<tr>
<td>Cutaneous</td>
<td>16</td>
<td>40</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>22</td>
<td>55</td>
</tr>
<tr>
<td>Pallor</td>
<td>16</td>
<td>40</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>21</td>
<td>43</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>9</td>
<td>23</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>14</td>
<td>35</td>
</tr>
</tbody>
</table>

**Table 1. Baseline characteristics of patients (n = 40)**

**Table 2. Response Rates**

**Table 3. Hematological and non-hematological toxicities (n = 40)**
Discussion

Metastatic breast cancer (MBC) remains essentially an incurable disease even with the availability of different chemotherapeutic and biological agents with < 10% of patients disease-free beyond 5 years. Treatment of patients with MBC using chemotherapy is mainly to relieve disease-related symptoms, to improve quality of life and to prolong survival [14]. It is wise to try to achieve a significant symptom improvement beside high response rates but not at the expense of substantial adverse effects. The rationale for combining gemcitabine and docetaxel included: (i) their potent mechanism of action with different intracellular targets; (ii) both drugs have a high level of single activity in MBC[15,16]; and (iii) promising and encouraging results of some phase I/II trials evaluating this combination as first and second-line therapy in ABC[17, 18]. The results of our study showed that the combination of docetaxel and gemcitabine is a highly active and well tolerated regimen in first-line therapy of naïve patients with MBC.

In the current study, ORR was recorded in 26(65%) patients [95% confidence interval (CI) 56% - 80%]; where 4(10%) patients attained CR; 22(55%) patients attained PR. Stable disease (SD) occurred in 8(20%) patients and 6(15%) patients had PD. These response rates are almost similar to that reported in the study conducted by Kornek et al [19] who evaluated 52 patients with MBC; they reported that ORR was 61% for patients who had not received prior chemotherapy for metastatic disease [95% confidence interval, 43.4–75.9%], they reported that ORR was 61% for patients who had not received prior chemotherapy to the current study, myelosuppression was occurred in the form of grade 1/2 neutropenia in 20(50%) patients and grade 1/2 anemia in only one (2.5%) patient. Some cases needed to use G-CSF as a therapeutic maneuver for neutropenia and despite the reported neutropenia there was no reported cases of febrile neutropenia. While Kornek and his co-workers [19] documented that myelosuppression was the most common adverse reaction, as grade 1/2 anemia had occurred in 61% of the 52 enrolled patients and grade 1/2 neutropenia had occurred in 50% of their patients, while the most common non-hematological toxicity in their study was nausea and vomiting which had occurred as grade 1/2 in 58% patients followed by grade 1/2 alopecia in 37% of the enrolled patients. In the study conducted by Chan et al [21], hematological toxicities were severe as grade 1/2 anemia occurred in 93% of the cases, 84% of the patients had developed grade 3/4 neutropenia, while alopecia in 68% of their patients and grade 1/2 nausea and vomiting in 46% of their studied patients.

Conclusion

In conclusion, gemcitabine in combination with docetaxel (given on days 1 and 15) has demonstrated an acceptable activity as well as a well tolerable safety profile. Further evaluation of this regimen is warranted in the treatment of patients who are chemotherapy naïve metastatic breast cancer as a first line.

References

Breast Cancer experience at Fakous Cancer Center (FCC)

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Abstract

Background: Breast cancer (BC) is the most important cancer in women in an increasing number of developing countries. Objectives: To measure that improving public awareness, education and training primary health care achieve down staging of breast cancer in a rural district in Egypt.

Subjects & Methods: 1-Education & training of primary health care providers. 2- House to house survey. 3- Women campaigns. 4- Barriers for early detection of BC were investigated.

Results: we interviewed 16166 women and found the most frequent age group was 30-39 ys (27.9%), 52% had early menarche, no breast feeding 59% among the multipara women, 54% were overweight, 86.5% of the menopausal women had delayed menopause and Illiteracy (34.5%). The prevalence of BC during 2007-2008=1.7 per 1000 examined women. Analysis of 1425 patients with mastectomies we found increase in the number of BC per time. T2 & T1 (53.5% & 19.8%) during 2004-2008 and (47.8% & 8.8%) during 1992-2003. Reluctance in seeking medical care (56.9%), far distance from health services (56%), negligence of the complaint (47.5%), and fear from BC diagnosis (44.2%).

Conclusions & recommendations: we recommended the need for planning health education programs on a wide scale on the studied villages to improve not only awareness, or knowledge but also changing the faulty attitudes & practices about BC especially among illiterate & low socioeconomic women. Proper training of health care providers at primary health care units. Phase II study in the remaining 52 village to cover the whole area was suggested.

The authors declare that there are no competing interests. This research paper was financed totally by the authors of the study.

Introduction

Breast cancer is the most important cancer in women in an increasing number of developing countries. In the Eastern Mediterranean region, breast cancer is by far the most common cancer even when considering men and women together, with 2 time more cases (N=57 000 new cases per year) than lung cancer (N=25 000) or bladder cancer (N=25 500). Of the available cancer control measures for breast cancer, primary prevention, screening and improved therapy, only screening has the potential for a rapid and major effect though this will be restricted to a reduction in mortality rather than a reduction in incidence. Of the available screening tests, mammography, physical examination of the breasts and breast self-examination, only mammography is established as effective in reducing mortality from breast cancer. However, mammography requires expensive technology, highly trained radiologists and radiographers, and is out of reach for most developing countries. Further, in women under age 50 there is little evidence for a benefit, and if a benefit exists, it is less than in older women.

Preliminary result about down staging programs based on clinical breast examination (CBE), breast self examination (BSE), public awareness campaigns and training of primary health staff have shown very encouraging results in different low-income countries settings, for example urban Egypt and Borneo Island.

Data from the regional population-based cancer registry at Gharbia governorate 2000-2002 (Egypt) as well as data from the National Cancer Institute hospital based registry (Cairo) show that breast cancer is the first cancer in Egypt (19% of all cases, male and female considered together). It is by far the commonest cancer among Egyptian women and represents 37% of all female cancers. Incidence in term of crude Incidence and age standardized rate are relatively high for a low income country (37.6 / 100,000 and 49.6 / 100 000 respectively).

The aim of this study was to measure in which extends a program that improves women’s awareness, and training of primary health care providers about early detection of breast cancer, clinical breast examination & teaching women how to do self breast examination would achieve downstaging of breast cancer in a rural district in Egypt (i.e. the Fakous district in the Nile delta region). With specific objectives: explore the most important risk factors of breast cancer, and determine prevalence of breast cancer in addition to determining the most frequent barriers of delay in breast cancer diagnosis.
Subjects and Methods

Downstaging program was started since the year 2004. A training team composed of a radiologist, a clinical oncologist, a nurse, a palliative care specialist and surgeon specialist of clinical breast exam (CBE) has provided education and training courses about theoretical and practical aspects of breast cancer that were held at Fakous Cancer Centre for the health care providers (HCP); (primary health care doctors, 2-3 nurses) and health visitor 4-6 volunteers from each included village. The trainees were made aware on the most important risk factors, importance of early detection & treatment with emphasis on cure for early-stage disease and good palliative care for later stages. The main objective of the training was to ensure proper mastery of different techniques: clinical breast examination (CBE), teaching breast self-examination to women. This training was boosted regularly every month before starting data collection. Volunteers were included in this study to encourage community participation. Inclusion criteria were volunteers should be highly educated, relatives of breast cancer cases or breast cancer survivors, inhabitants of the selected villages to be more familiar with the interviewed women (N.B. non-employee received relocation allowance).

The study was conducted on rural region of Fakous District. Large scale survey house to house for two years (2007-2008) was held to cover 21 villages that were divided into 9 regions (A, B, C, D, E, F, G, H, & I) according to the related local units. Then, interventions by health education about; early detection of breast cancer, how to do SBE, and investigations (mammogram, ultrasound, & fine needle biopsy) were done for the suspected cases.

The primary data were collected by a questionnaire which was designed for collecting the data of the survey of the program. It was prepared to ask women about some sociodemographic characteristics, and risk factors of breast cancer (BC) as; age, residence (village or Ezba), education, marital status, no of family members, no of rooms, age of menarche, age of 1st full term pregnancy, no of children, history of breast feeding, age of menopause if present, family history of breast cancer, or any history of breast complaint. In addition to any suspected symptoms of breast cancer as lump, pain, tenderness, or nipple discharge. Weight and height were measured by weighing scale & stadiometer. Body mass index (BMI) was calculated for every interviewed women using the formula [weight(kg)/height(meters)^2]. The questionnaire was pretested before use for any modification. Another questionnaire was also applied on the breast cancer patients who had admitted at FCC (2004-2008) to explore some social, psychological, or economical barriers about causes of late diagnosis of breast cancer. In addition to, knowing the tumor size (T1, T2, T3, & T4), and the stage of the tumor (stage I, II, IV, & UV) according to TNM Staging system.

The program also included strengthening of public awareness. This was achieved by distribution of pamphlets or brochures and posters in their local languages that aimed at motivating patients to go to the nearest rural health clinic if specific breast symptoms were present. In addition, as part of their routine duties, the trainees nurses were instructed to hold a health education talk and discussion on the subject during one of their monthly visits to the villages . During these visits they would teach the villages’ women about the early signs and symptoms of breast cancer. Breast self-examination was taught to all women. Preparing places for women meeting campaigns at the studied villages for clinical breast examination that was carried out when women were agreeable by primary health care doctors with the help of the training team from FCC. Then, referral of the suspected cases to FCC for doing mammogram, ultrasound, and fine needle biopsy to ensure the diagnosis. The budget used for this program was for health staff training (mainly for the travel cost for the trainers, salaries are excluded) and for pamphlets and posters.

The secondary data were collected from the statistical records of breast cancer at FCC from 1992-2008 and reviewed as regards to tumor size, stage of tumor, & lymph nodes enlargement. Evaluation of the downstaging program was done by analysis of the collected data either primary or secondary.

Ethical considerations were taken into account as oral consent from each woman before the beginning of the study. Approval from the related health authorities was taken also.

Data manipulation

Data entry was carried out by using SPSS software version 13 that was preceded by revision, coding, & develop checking of the data in order to minimize errors during its entry. Data analysis; tabulation, and graphic presentations as well as simple statistical analysis were carried out. Interpretation and commenting were done, in addition to discussion of the findings.

Results

The trainees’ team had interviewed a total sample of 16166 women [9933 in the year 2007 and 6233 in 2008] at the survey in the studied 21 villages. As regards to some sociodemographic characteristics and risk factors of BC, the most frequent interviewed age groups were 30-39 ys, 20-29 ys, and 40-49 ys (27.9%, 24.9%, and 22% respectively) with mean Age (years) ± SD (38.7 ± 12.0). The highest percentages of crowding index CI were 3-4 persons /room and ≥5 persons /room (45.8% & 32.7% respectively). About 52% of the studied females had early menarche (<12 years). Null parity constituted 4% of the studied sample. The age of women at 1st full term pregnancy (at ≥35years) represented more than one quarter (26.6%) of the studied females. In addition to no breast feeding which constituted 59% among the multipara women. More than 54% of the studied sample was overweight and obese. Positive family history of breast cancer constituted 3.5%. About 86.5% of the menopausal women had delayed menopause (≥50 years). Illiteracy took the upper hand among the studied females (34.5%) as shown in (table 1).

After doing clinical breast examination (CBE) for the women with breast conditions (1200 women) at outpatient clinic of the included primary health care units during 2007-2008, it was found that 28 cases of cancer breast (2.3%) were discovered and diagnosed after doing the proper investigation (mammogram, ultrasonography, and histopathological report) and 71 cases with benign breast lesions (5.9%) as illustrated in (Figure 1). The prevalence of cancer breast during 2007-2008=1.7 per 1000 examined women as shown in (table 2). And after doing histopathological reports for the discovered BC cases, it was found that the frequent tumor sizes were T2 (55.5%) and T3 (22.2%) followed by T1(11.1%) and T4 (11.1%) (Figure 2)

After analysis of the statistical records of 1425 patients with mastectomies which were done at FCC between 1992 and 2008 had showed that there was an increase in the number of breast cancer per time as illustrated in the linear diagram (Figure 3).

It was noticed that patients presented with infiltrating duct carcinoma (IDC) histopathology represented the most frequent percentage (62.3%) as shown in (table 3). However, T2 & T3 were the frequent tumor sizes among the studied records 1992-2008 (34.7%, & 26.4% respectively). More than two thirds of the studied patient’s record had lymph node metastasis. Mean tumor size was 3.9 cm. Distribution of breast cancer to benign lesions in the breast among the studied records from 1992-2008 had showed that benign lesions represented 49% while breast cancer represented 51% (from histopathological reports) as shown in pie diagram (Figure 4).
By reviewing the BC stages among the patients’ records with BC from Fakous district in 2004-2008 at FCC, it was found that the most frequent tumor stages were stage II (41.1%), stage III (31.9%) followed by stage IV (7.0%) & stage I (6.6%) as in (table 4).

Comparing mean age & size of tumor among the studied records of cases of breast cancer at 1992-2003 & 2004-2008 shows that there is significant difference between the two studied periods as regarding to age & tumor size (p=0.045 & p=0.001 respectively) (table 5 & table 6). The most frequent tumor size were T2 & T1 (53.5% & 19.8% respectively) during 2004-2008 as compared with that during 1992-2003, T2 & T1 (47.8% & 8.8% respectively).

By analyzing the data of the questionnaire to BC patients at FCC that was done to understand the social, psychological and economical barriers to early diagnosis and treatment among Fakous population and the most important determinants of late presentation. Reluctance in seeking medical care (56.9%), far distance from health services (56%), negligence of the complaint (47.5%), and fear from BC diagnosis (44.2%) constituted the most frequent barriers for early detection of breast cancer among the patients with breast cancer (table 7).

Discussion

This work described that there were high percentages of multiple risk factors for breast cancer among the interviewed women during survey as (early menarche, delayed menopause, late age at fist birth, little or no breast feeding, overweight & obesity, in addition to family history). These findings agreed with that reported by Albrektsen et al & Lipworth et al who explored the interaction between these risk factors and breast cancer.

Low socioeconomic status and illiteracy constituted important precipitating factors of lack of awareness and knowledge of these women about the breast cancer especially if complaining from breast conditions.

One in eight women and one in four women develop breast cancer in the US and the UK respectively, and Egypt follows closely behind the UK’s prevalence rate. Prevalence of breast cancer at this work was 1.7 per 1000 women. Although this prevalence was high but still underestimated as many women refused to be examined or unavailable at house during the survey time. Boulos et al revealed that about eight breast cancers per 1,000 women were found after the screening program in the first year, and when half the women were contacted again in the second year, two cancers per 1000 women were detected.

Unfortunately, it was noticed that about 77.7% of the discovered cases with breast cancer had tumor sizes T2 & T3, which indicated late diagnosis and denial of the women to be discovered early that would be reflected on their survival rate later on. In addition to the lack of mass screening programmes in these marginalized rural areas.

In many developed countries, organized mammography screening is available at the population level while developing countries lack such facilities. An ideal screening test for developing countries needs to be simple, inexpensive and effective. Mammography is far from reaching these criteria. Hence, breast self-examination and clinical breast examination (CBE) to detect any abnormalities have been envisaged as alternatives. There are indications that good clinical breast examinations by specially trained health workers could have an important role especially in women under 50.

By reviewing the number of cases of BC admitted at FCC during the period from 1992-2008 with marked increase in the number of cases with time. Breast cancer is an urgent public health problem in high-resource regions and is becoming an increasingly urgent problem in low resource regions, where incidence rates have been increasing by up to 5% per year.

This work revealed that the leading tumor histology in all registries at FCC was infiltrating duct Carcinoma (IDC), followed by lobular carcinoma (ILC). These findings were in accordance with Anderson et al.

The incidence of breast cancer is lower in developing countries than in developed countries, but the stage at presentation is much later. T2 & T3 took the highest percentages among tumor sizes with lymph nodes metastasis in the reviewed records at FCC 1992-2008. But the previous results may differ with that of Maailej Met al. 2008 (Tunisia)(14), CH Yip 1996 (Malaysia)(15), and university hospital, kuala lumpur who reported that T2 & T4 were the frequent tumor sizes in their studies.

Stage II & stage III of the tumor were the most frequent among the studied cases of BC at FCC 2004-2008, which were consistent with that found by Ezzat AA et al, Saudi Arabia & Bedwani et al 2001 Alexandria. While these were different from that reported by Cairo project (all Egypt), which revealed that stage II, IV, & III were the most frequent tumor stages.

The low incidence of inflammatory breast cancer (0.3%) in our series proved to be an underestimated value due to the fact that many of these cases were clinically misdiagnosed as locally advanced breast cancer rather than true inflammatory cases. Diagnosis of inflammatory breast cancer remains a challenge and a subjective one. This was clearly evident in the joint work conducted at the National Cancer Institute (Cairo), the Salah Azaiz Institute (Tunisia) and the University of Michigan. The importance of tumor size in improving survival is increasingly evident, and recent evidence by Elkin et al has shown that measuring the impact of an early detection program by stage alone would fail to observe tumor downsizing benefits within stage groups.

The mean of the tumor size was smaller in the period 2004-2008 compared with that 1992-2003, in addition to frequent cases of BC with T1, & T2 at 2004-2008. This indicated that since the application of the downstaging program, there was improvement in the tumor size & stage. Considering some barriers for early detection of breast cancer among the studied cases at FCC, it was found that the highest percentage of the studied patients with mastectomies due to BC are illiterate which reflect their ignorance for awareness or knowledge about the breast cancer. In addition to reluctance in seeking medical care, far distance from health services, negligence of the complaint, and fear from BC diagnosis constituted another precipitating factors for delay in diagnosis. So this would increase both morbidity & mortalities from this terrible disease as described by people (it is considered a death sentence). It is estimated that 99% of Egyptian women are unaware of the dangers of breast cancer. Because of this lack of awareness, incidents of death from breast cancer are higher in Egypt than in other parts of the world. This is exacerbated by the fact that many people will not talk about cancer, nor are women educated to perform self-breast examinations and take mammogram tests. Unfortunately only highly educated women or those who have been overseas are aware that breast cancer if caught in the early stages, can be cured. Consequently women are coming to doctors when the cancer has reached an advanced stage, necessitating aggressive treatment.

There is also a common misconception in Egypt that cancer is contagious, a notion that has caused the husbands of many diagnosed women to seek a divorce. If a young woman is diagnosed with breast cancer, she is considered unmarriageable. Egyptian women do not usually come forward until the late stages of the disease, when it is often too late to assist.
Conclusions & recommendations

A key part of the fight against breast cancer is early detection, if treated in time the patient’s life can be saved. The downstaging program started at 2004 had showed the following benefits; exploration of the most important risk factors of BC, its prevalence, reduction of the tumor size at presentation, creation of an atmosphere of understanding and awareness about BC that improved the compliance of people, and built a relationship between health service provider and the marginalized areas. The most important barriers for late diagnosis of BC were recognized. Our results recommended the need for planning health education programs on a wide scale on the studied villages to improve not only awareness, or knowledge but also changing the faulty attitudes & practices about breast cancer especially among illiterate & low socioeconomic women. Proper training of health care providers at primary health care units about the importance of CBE in early detection of BC cases especially in low resources settings, beside taking the women’s complaints seriously. Phase II study in the remaining 52 village to cover the whole area was suggested.

Tables

Table 1. Percentage distribution of breast cancer risk factors among the interviewed women during survey (no=16166).

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age groups:</td>
<td></td>
</tr>
<tr>
<td>&lt;20 years</td>
<td>1.1</td>
</tr>
<tr>
<td>20-29 ys</td>
<td>24.9</td>
</tr>
<tr>
<td>30-39 ys</td>
<td>27.9</td>
</tr>
<tr>
<td>40-49 ys</td>
<td>22.0</td>
</tr>
<tr>
<td>50-59 ys</td>
<td>12.9</td>
</tr>
<tr>
<td>≥ 60 ys</td>
<td>11.2</td>
</tr>
<tr>
<td>Illiteracy</td>
<td>34.5</td>
</tr>
<tr>
<td>Age at 1st full term pregnancy:</td>
<td></td>
</tr>
<tr>
<td>At ≥35 years</td>
<td>26.6</td>
</tr>
<tr>
<td>No breast feeding</td>
<td>59.0</td>
</tr>
<tr>
<td>Delayed menopause (≥50 years)</td>
<td>86.5</td>
</tr>
<tr>
<td>Early menarche (&lt;12 years)</td>
<td>52.0</td>
</tr>
<tr>
<td>Overweight and obesity</td>
<td>54.5</td>
</tr>
<tr>
<td>Null parity constitutes</td>
<td>4.0</td>
</tr>
<tr>
<td>Positive family history of cancer breast</td>
<td>3.5</td>
</tr>
</tbody>
</table>

Table 2. Number of women with positive breast cancer during house to house survey 2007-2008.

<table>
<thead>
<tr>
<th>Region</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
<th>H</th>
<th>I</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of women (Central Agency for Public Mobilization &amp; Statistics CAPMAS)</td>
<td>14660</td>
<td>17851</td>
<td>10100</td>
<td>18785</td>
<td>8101</td>
<td>12504</td>
<td>10724</td>
<td>10530</td>
<td>11801</td>
<td>115056</td>
</tr>
<tr>
<td>No. interviewed women by the trained team during survey</td>
<td>1077</td>
<td>1141</td>
<td>1618</td>
<td>2142</td>
<td>921</td>
<td>2565</td>
<td>3767</td>
<td>1448</td>
<td>1487</td>
<td>16166</td>
</tr>
<tr>
<td>No of women with Positive breast cancer</td>
<td>3</td>
<td>6</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>28</td>
</tr>
<tr>
<td>Prevalence of cancer breast at the studied regions</td>
<td>28/16166 X 1000=1.7 per 1000 women during 2007-2008.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Pathological type of the tumor, its size & the involved lymph node enlargement among the studied records of breast cancer (1992-2008).

<table>
<thead>
<tr>
<th>Variable</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathological Type:</td>
<td></td>
</tr>
<tr>
<td>IDC</td>
<td>62.3</td>
</tr>
<tr>
<td>ILC</td>
<td>13.4</td>
</tr>
<tr>
<td>DCIS</td>
<td>10.3</td>
</tr>
<tr>
<td>IBC</td>
<td>0.3</td>
</tr>
<tr>
<td>OTHERS</td>
<td>13.6</td>
</tr>
<tr>
<td>Tumor size:</td>
<td></td>
</tr>
<tr>
<td>Mean tumor size ± SD</td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>3.9 ± 1.1</td>
</tr>
<tr>
<td>T2</td>
<td>18.1</td>
</tr>
<tr>
<td>T3</td>
<td>34.7</td>
</tr>
<tr>
<td>T4</td>
<td>26.4</td>
</tr>
<tr>
<td>Lymph Node:</td>
<td></td>
</tr>
<tr>
<td>1-3</td>
<td>35.5</td>
</tr>
<tr>
<td>4-9</td>
<td>18.7</td>
</tr>
<tr>
<td>≥ 10</td>
<td>14.9</td>
</tr>
<tr>
<td>-ve</td>
<td>14.2</td>
</tr>
<tr>
<td>NX</td>
<td>16.7</td>
</tr>
</tbody>
</table>

Table 4. Percentage distribution of tumor stage among the studied patients’ records with cancer breast 2004-2008 (no=682).

<table>
<thead>
<tr>
<th>Tumor stage</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>6.6</td>
</tr>
<tr>
<td>Stage II</td>
<td>31.9</td>
</tr>
<tr>
<td>Stage III</td>
<td>41.4</td>
</tr>
<tr>
<td>Stage IV</td>
<td>7.0</td>
</tr>
<tr>
<td>Stage UN</td>
<td>12.8</td>
</tr>
<tr>
<td>Total</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 5. Comparing tumor size between cancer breast cases registered at 1992-2003 and 2004-2008 from records at FCC.

<table>
<thead>
<tr>
<th>Tumor size</th>
<th>1992-2003 (no=726)</th>
<th>2004-2008 (no=682)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>64</td>
<td>135</td>
<td>0.000</td>
</tr>
<tr>
<td>T2</td>
<td>347</td>
<td>365</td>
<td>53.5</td>
</tr>
<tr>
<td>T3</td>
<td>164</td>
<td>81</td>
<td>11.9</td>
</tr>
<tr>
<td>T4</td>
<td>111</td>
<td>44</td>
<td>6.5</td>
</tr>
<tr>
<td>TX</td>
<td>40</td>
<td>57</td>
<td>8.3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>1992-2003 (no=732) Mean ± SD</th>
<th>2004-2008 (no=624) Mean ± SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (ys)</td>
<td>46.3 ± 11.4</td>
<td>47.6 ± 13.4</td>
<td>0.045</td>
</tr>
<tr>
<td>Size</td>
<td>4.2 ± 2.6</td>
<td>3.6 ± 1.8</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Table 7. Social, psychological, or economical barriers about delay in early detection of breast cancer in BC patients at FCC (2004-2008).

<table>
<thead>
<tr>
<th>Barrier</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negligence of the complaint</td>
<td>47.5</td>
</tr>
<tr>
<td>Reluctance in seeking medical advice</td>
<td>56.9</td>
</tr>
<tr>
<td>Fear from BC diagnosis</td>
<td>44.2</td>
</tr>
<tr>
<td>Lack of time</td>
<td>23.6</td>
</tr>
<tr>
<td>Far distance from health services</td>
<td>56.0</td>
</tr>
<tr>
<td>Patient poverty &amp; High cost</td>
<td>27.8</td>
</tr>
</tbody>
</table>

Figures

Fig 1. Percentage distribution of the type of breast lesion among the examined females during survey.

Fig 2. Bar chart; percentage distribution of the size of the tumor among the discovered cases of BC in the studied females during survey.

Fig 3. Line diagram shows the trend of breast cancer cases at FCC during the studied period 1992-2008.

Fig 4: Percentage distribution of type of breast lesions among the studied records at FCC (1992-2008).

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Long Survival of Metastatic Breast Cancer in center of Tunisia, about 34 cases


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Key words: Cancer, breast, woman, metastatic, long survival.

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Abstract

Breast cancer is the most common cancer for women. Survivals protruding 5 years are rare.

Our retrospective study was about 34 patients with metastatic breast cancer surviving more than 5 years who were supported at the department of medical oncology in Farhat Hached Hospital between January 1994 and December 2011. The aim of our study was to identify clinic pathologic characteristics, treatment and prognostic factors for long survival of women with metastatic breast cancer. The average age at diagnosis of metastases was 53ans. The tumor was classified as T3-T4 in 64.6% of cases. Infiltrating ductal carcinoma was found in 85.3% of cases. Nearly 80% of tumors were grade II or III SBR. Hormone receptors were positive in 88.2% of the cases. Thirteen patients had metachronous metastases (38.2%) and 21 had synchronous metastases (61.8%). Bone metastases were the most frequent (82.3%). The recurrence-free interval was 51.5 months. Twelve patients (92%) with metachronous metastases and 21 patients with synchronous metastases underwent palliative chemotherapy with a median time to progression of 6 to 25 months. 30 patients underwent palliative hormone therapy (20 in the case of synchronous metastases and 10 cases of metachronous metastases) with a median time to progression of 13 to 35 months. The median overall survival was 100 months. The median survival was 75 months metastatic. Prognostic factors for survival were a long clinical size of the tumor (T1 and T2) and hormone receptor negative.

In recent years, new treatments associated with the evaluation of new strategies, show significant improvement in survival in metastatic breast cancer.

Introduction

Breast cancer is the leading cancer for women worldwide [1]. In Tunisia, according to three registers in the country (north, center and south), it ranks first cancers woman with respective frequencies of 30%, 31% and 31% [2]. It remains a public health problem.

Although recent advances have led to improved prognosis of this cancer, thanks to advances in screening and adjuvant therapy, some forms mainly metastatic disease remain poor in prognosis. Indeed, 6-10% of patients present with synchronous metastases and 30% of patients initially nonmetastatic develop metachronous metastases during the course of their disease with a maximum peak of relapses which is between 2 and 3 years [3]. Metastatic breast cancer remains an incurable disease in the majority of cases. Therapeutic progress, both in terms of chemotherapy targeted therapies have certainly prolonged the survival of these patients, but the long survivals are rare. In this work, we present a series of 34 patients with metastatic breast cancer and surviving more than 5 years.

The objectives of this work are to clarify clinical, pathological and therapeutic features and to identify prognostic factors in this series.

Patients and methods

Our retrospective study over a period of 17 years (January 1994-September 2011). It involved 34 patients with breast cancer diagnosed and histologically proven.

These patients presented either synchronous metastases (MS) [at the time of initial diagnosis] or metachronous metastases (MM) occurred at any time after the initial treatment.

Overall survival over five years from the initial diagnosis of secondary locations. The dependent variables studied were survival and duration of response. Survival was calculated from the date of diagnosis of metastases to the date of last news for patients with synchronous metastases and from the date of metastatic relapse up to date with the latest news for patients’ metachronous metastases.

The duration of response was calculated from the date of the beginning of the treatment of metastatic disease to the date of progress or death of patients.

The study of survival is calculated according to the Kaplan-Meier method and comparison of different rates of survival by log-rank test, a value of p ≤ 0.05 was considered statistically significant.
Results

Clinical and pathological characteristics
The age of our patients was between 30 and 79 years with an average of 53 years. The tumor was classified as T4 in 16 cases (47%), T3 in 6 cases (17.6%), T2 in 9 cases (26.6%) and T1 in three remaining cases (8.8%). The clinical nodal involvement was observed in 53% of cases. The histological type was the most common invasive ductal carcinoma in 85.3% of cases. The SBR histologic grade was high (II or III) in 79.4% of cases. Hormone receptors were positive (ER + and / or PR +) in 88.2% of cases. HER2 status was performed in 2 patients by immunohistochemistry and was not expressed in the two cases. Thirteen patients had metachronous metastases (38.2%) and 21 had synchronous metastases (61.8%).

The mean time to relapse was 51.5 months with a range of 17 to 132 months. Relapse had occurred after the first 2 years in 92.3% of cases.

Relapse diagnosis was made before clinical symptoms for 9 of our patients. Bone pains were the most frequent presenting symptoms synchronous metastases (42.8%) and metachronous metastases (53.8%).

Bone metastases were more frequent in patients with synchronous metastases (90%) and in patients with metachronous metastases (69.2%), followed by lung and liver secondary.

Six patients with synchronous locations.

Therapeutic results
All patients with metachronous metastases had undergone surgery for their primary tumor. It was Patey type in 69.2% of cases and conservative in 23.1% of cases. Metastases underwent surgery of their primary tumor. It was Patey type in 4 cases (after correct answer metastases palliative chemotherapy in one patient and before complete staging by bone scintigraphy in the other 3 patients) and mastectomy clean in two remaining cases.

Two patients had received surgery for osseous metastases secondary. The first patient had a consolidation surgery of the bone after a pathologic fracture and the second patient had a spinal surgery (laminctomy) for spinal cord compression.

The first-line chemotherapy was essentially based on anthraclylines in 27 cases (81.8%), taxane in 2 cases (6%) and based CMF (cyclophosphamide-methotrexate-endoxan) in 3 cases (9%). After the first line palliative chemotherapy, the objective response rate, all protocols together for synchronous and metachronous metastases were 57.8% and the average duration of response was 11.9 months.

Twenty-three patients underwent palliative chemotherapy second-line. This was taxane in 11 cases (47.8%), based on vinorelbine in 10 cases (43.6%), based on platinum in 1 (4.3%) and base mitomycin-vinblastine in the remaining case (4.3%). The objective response rate, all combined protocols for synchronous and metachronous metastases were 47.8% and the average duration of response was 13.6 months.

Thirteen patients underwent palliative chemotherapy third line. This was based on vinorelbine in 6 cases (46.1%), taxane in 6 cases (46.1%) and based capecitabine in the remaining case (7.8%). The objective response rate after chemotherapy, all protocols combined was 30.7%.

Six patients underwent palliative chemotherapy fourth line. She was based in 3 cases capecitabine and CMF-based in three remaining cases. The objective response rate after chemotherapy, all protocols combined was 16.7%.

Thirty patients underwent palliative first-line hormone therapy, either immediately at diagnosis of metastases after failure of either relay or response to palliative chemotherapy. It was essentially based on tamoxifen in the majority of cases (70%). The objective response rate in the first-line metastatic hormone of all types, was 50%. While the average duration of response was 23 months in the case of synchronous metastases and 35 months for metachronous metastases.

Hormone palliative second line was used in 20 of our patients. It was based on anti-aromatase such 2nd generation steroidal or non-steroidal in most cases (85%). The objective response rate to hormone palliative second line of all types was 55%. While the average duration of response was 11.3 months.

Of the 28 patients who presented with bone metastases, 21 had bisphosphonates (75%). The median duration of bisphosphonate prescription was 49 months for metachronous metastases and 22.5 months in the case of synchronous metastases.

Radiotherapy was bone analgesic in 14 cases, for decompressed spinal cord compression in 1 case, after loco regional palliative surgery of the primary tumor in 2 cases and loco regional recurrence in cervical lymph node metastasis in 2 cases.

Study of survival
The median overall survival was 100 months, with a range from 60 to 221 months (Fig 1) and the median survival from diagnosis of metastases was 75 months, with a range from 60 to 162 months (Fig 2).

Patients classified as T1 and T2, TNM malignant tumors (UICC / AJCC) had a better survival than patients classified as T3 and T4. The difference was statistically significant with p = 0.05 (Fig 3). The median survival of patients classified as T1 or T2 was 162 months versus 68 months for patients classified as T3 or T4.

Other factors influencing survival were not statistically significant: age, menopausal status, clinical nodal involvement, histological type, grade SBR, Nature metastatic site, the chronology of metastasis and response to palliative chemotherapy.

Evolution
Of the 34 patients in our series and date update medical records (01 September 2011):

- Twenty-three patients died due to progression of metastatic disease.
- Ten patients are still alive:
  - Two of them are in complete response.
  - Five women are stable.
  - Three women are in metastatic progression.
- One patient was out of sight, she was in complete remission at the time of her latest news.

Discussion
Breast cancer is the most common cancer for women. It is a major problem of public health. Its incidence increases significantly over the past three decades in the United States and Western Europe [4]. Moreover, it’s the most common cause of death from cancer for women.

In Tunisia, breast cancer is the most common cancer for women. It represents about 30% of female cancers. Unfortunately, the diagnosis is still at a late stage. In Tunisia, the frequency of metastatic breast cancer at diagnosis in a series of Tunisian center until the year 1996 was 15.4%. The rate was 13.1% in the north of Tunisia until 2004 according to the study Maalej et al [5] However, in southern Tunisia, the incidence was 9.6% until 2007.

In Western countries, this rate varies between 6% and 10% [6]. The proportion of patients who will develop metastases secondary is around 30% [3]. Currently, the median survival of metastatic breast cancer is between 18 and
30 months [7]. The notion of long-term survival is not clearly defined in the literature. Our choice of 5 years followed after the diagnosis of metastases was arbitrary.

Several studies have focused on analyzing the prognostic impact of patient age of diagnosis of metastases on survival.

Long survival beyond 5 years are more common in young women, as proved by the series of German Cnossen [8] and the Danish series Ryberg [9]. In our series, the survival of patients whose age was <50 years was slightly better than that of other patients, but the difference was not statistically significant.

Dawood et al [3] showed that long-term survival rate was higher in premenopausal women with a median survival of 45 months (range: 37-64) against 38 months in postmenopausal women (range: 33-42).

In our series, the survival of premenopausal women was better than postmenopausal but the difference was not statistically significant.

Cnossen et al [8] showed that long-term survival rate was higher in tumors classified as pT1 or pT2 with a median survival of 53 months (range 37-69) months against 34 tumors classified pT3 or pT4.

In our study, the clinical size was a prognostic factor determining the long-term survival (p = 0.05).

In the German series of Cnossen et al [8], women without lymph node involvement (N-) with a longer survival (median survival 57 months, with a range from 41 to 73 months) compared to the population N+ (median survival 38 months, with a range from 32 to 44 months).

In our series, survival between the 2 groups in clinical N0 and N+ was almost identical. The difference was not statistically significant.

Histological type did not influence survival in metastatic. Long survivals are described for both the CLI ITC [10].

In the Danish series of Hietanen et al [11], the rate of long-term survival beyond 5 years was higher in patients with SBR grade I (24%) compared with patients with a high grade SBR (12%).

In our series, patients with SBR grade I had a better survival than those with a high grade (II or III), but the difference was not statistically significant.

It is clearly recognized that the expression of hormone receptors by the tumor is associated with longer survival [12]. The estrogen receptor and / or progesterone were expressed in 88.2% of our patients. This frequency was similar to that described in a retrospective study German [19], focusing on the long survival in metastatic breast cancer where the rate of RH+ was high (78%).

According to the literature, 20% of patients with breast cancer have HER2 overexpression status [3]. It was sought only in 2 of our patients and was not expressed in the two cases. Its overexpression is a poor prognostic factor [13,14]. The time of relapse is a prognostic factor and predictive of longer survival. In the Danish series Hietanen et al [11], the rate of long-term survival beyond 5 years was higher in patients with relapsed within>2 years (21%) compared with patients with a short delay <2 years (15%).

Some studies have shown that the prognosis of synchronous metastases is better than metachronous metastases. Dawood et al [3] found that the median survival of women with MS was 12 months longer than women in relapse of their disease. The rate of long-term survival beyond 5 years was higher in case of synchronous metastases: 32% versus 22% for metachronous metastases.

Our study did not confirm these data and the difference in survival between the two groups was not significant.

Survival in breast cancer with bone metastases is generally longer than for other metastatic sites: median survival is between 24 and 48 months [15, 16]. Long survivals are also common with 20% surviving beyond 5 years [16].

Several recent studies have shown that surgical treatment of the primary tumor significantly improves overall survival of patients with metastases. Three of them have shown the benefits of this treatment on long survival beyond 5 years [17, 18], such as the series of Ruiterkamp et al [19] where the rate of long-term survival with surgery of the primary tumor was 24.5%.

Long survival in metastatic breast cancer, described through literature, are obtained after an objective response (complete or partial response) to several lines of chemotherapy and / or hormone therapy if the tumor is hormone [19, 20]. This was the case in our series. Long survival beyond 5 years caused by a single line of chemotherapy or hormone therapy are extremely rare [21].

In a prospective study internationally, the rate of long-term survival (beyond 5 years) was 16% among women who were treated with anthracyclines Protocol (FAC) against 5% when using the CMF protocol [22].

In our series, these protocols (FAC or FEC) used in first-line metastatic gave an average rate of objective response of 59%, a complete remission rate of about 11% and a median time to progression of 10.7 months.

Taxanes are often used either as mono therapy or in combination with other cytotoxic agents in the treatment of metastatic breast cancer. A review of 21 randomized trials in 2005 showed the superiority of chemotherapy regimens containing taxanes compared to other types of chemotherapy, in terms of objective response rate and overall survival [23]. As for HRT, several trials randomized showed that RNs are more effective than tamoxifen in first-line metastatic with objective response rates higher and longer response times ranging from 8.2 to 11.1 months as against 5.6 to 8 months tamoxifen [24,25]. Trastuzumab can extend survival in metastatic breast cancer over expressing HER2, as shown in a recent French study [26] where the rate of long survival beyond 7 years in patients treated with trastuzumab in the first line metastatic in combination with chemotherapy was 17%.

Few studies in the literature have examined the impact of palliative loco regional radiotherapy on overall survival of patients with breast cancer metastatic immediately. Scodan et al [27] showed the benefit of local therapy (which was essentially an exclusive irradiation therapy in 78% of cases associated with surgery in 13% of cases), overall survival at 3 years without any real benefit in the long survival beyond 5 years.

**Conclusion**

Metastatic breast cancer is incurable at present. The disease progresses by successive bouts and remissions are shorter and shorter as and measurement of exhaust treatment. But in recent years, advances in treatment because of new treatments associated with the evaluation of new strategies, show significant improvement in survival. The long-term survival in metastatic breast cancer necessarily entails progress in the field of palliative care. Palliative care and support are multidisciplinary physicians, nurses, psychologists, physiotherapists, social and educational assistants are particularly called upon to intervene and coordination is essential. They cater to the patient as a person, and his family, at home or in an institution.
Figures

1. Fig 1. Overall survival according to Kaplan-Meier

2. Fig 2. Survival from diagnosis of metastases

3. Fig 3. Survival according to clinical size

References


Metastatic phyllodes tumors: a case series

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Key words: Phyllode tumors, distant metastases, breast cancer.
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Abstract

Introduction: Breast Phyllodes Tumors are rare entities, however distant metastases are exceptional. Their management is not codified. The aim of these cases study was to describe this metastatic rare disease and their management.

Cases presentation: Three women aged 30, 68 and 38 were treated in the National Institute of Oncology in Morocco for metastatic breast phyllodes tumors. Two of them died rapidly due to the rapid growth of the disease.

Conclusion: Metastatic tumors have a poor prognosis with no long-term survival, death occurs within 24 months after the appearance of metastases, chemotherapy must be done as rapid as possible.

Introduction

Phyllodes tumors are fibro epithelial tumors. They are rare with a frequency ranging between 0.3 and 0.9 % of all breast neoplasma [1]. They occur at any age with a peak incidence between 35 and 50 years [1]. They recur in 24% to 58% of the cases. Distant metastases are exceptional. Few cases were reported in the literature.

Cases report

Case 1: A 30 years old female patient, presented a rapid increase in the left breast, combined with mastodynia, without axillary lymph node. Biopsy of the left breast showed a malignend phyllodes tumor. She underwent a left mastectomy without axillary node dissection. Frozen section confirmed diagnosis of Maligned phyllodes tumor. Adjuvant radiotherapy was performed.5 months later, the patient presented a mass of axillary and arm measuring 15x 18 cm. Workup including chest and abdominal CT scan showed bilateral diffuse lung metastases. The patient’s condition rapidly deteriorated, we began the supportive care. The patient died one month later.

Case 2: A 68 years old female patient who presented for 6 years a mass on the left breast, gradually progressing. Mammography showed nodular calcifications, cytology showed malignant cell. She had a tumorectomy with node dissection. Histology found malignant phyllodes tumor with negative nodes. Margins were negative. Two years later, the patient presented a local recurrence for which a mastectomy was performed. A year later a third recurrence occurred, revealing lung metastases. The patient died quickly of the evolution of the disease before starting chemotherapy.

Case 3: A 38 years old female patient underwent a wider lumpectomy. Histology showed phyllodes tumor grade 1. Margins were negative of tumor. Through evolution of the case, multiple recurrences occurred; they were treated by mastectomy after the first recurrence and surgical resection for the second and third recurrence. The patient also had radiotherapy. Four months later she presented an isolated lung metastatic reveled by CT scan of chest (figure 1) pathology demonstrated a metastatic phyllodes tumor (figure2) ,wish is actually proposed for surgical resection.

Discussion

Metastasis recurrence occur 2 to 5 years after diagnosis they are essentially localized at the level of lungs (60 to 70%) and bones (30%) [2]. Our patients had recurrence of metastatic lung occurring respectively at 9 months, 3 years, and 4 months after diagnosis.
Benign and malignant phyllodes tumors can recur locally and both have the potential to metastasize [2, 3]. Malignant lesions tended to recur earlier; they recur in 24% to 58% of cases, whereas benign phyllodes tumors recur only in 4.3% to 27% of cases [2, 3]. Surgery limits seems to be the main prognostic factor in terms of risk of local and metastasis recurrence.
The study by Mange et al [4] on 40 patients, and the study of Pandey et al [5] on 37 patients showed a significant association between the rate of local recurrence or metastatic and margins of resection when they are less than 10 mm. In the first case the limits of resection were marginal: 1 mm deep and 5 mm lateral to the patient presented a continuation evout local one month after the end of radiotherapy and metastasis 5 months later, to the second point of the limit ‘excision were healthy, local recurrence occurred 2 years after treatment, and
lung recurrence 3 years again later. Furthermore, tumor size (5cm) would also be a pejorative factor [6]. The correlation histopronostic has been reported as well: the existence of purely mesenchymal beaches “stromal overgrowth, the marked nuclear atypia and mitotic index greater than 3 to 4 / microscopic field (at magnification 400), are used as prognostic factors histology [2, 3].

Recent studies have revealed oncogenetics other prognostic factors: the gain of chromosome 1q and 4q12, loss of 13q [7], the expression of p53, mutation of the “epidermal growth factor receptor in the stroma [8]. Metastatic tumors have a poor prognosis with no long-term survival, death occurs within 24 months after the appearance of metastases. The treatment is based on chemotherapy, low response rates were observed in lung metastases and rarely with bone metastases. This joins the chemotherapy of breast sarcomas rather than carcinomas of the breast [9], based on protocols based ifosfamide alone or in combination with doxorubicin (dose above 60 mg / m²) [9]. Other agents such as cisplatin combined with doxorubicin and etoposide were used [1]. Despite the expression of hormonal receptors in phyllodes tumors, the role of hormone therapy is not established [10].

Conclusion

Metastasis recurrences are exceptional. Margins of resection and tumor size seem to be the main prognostic factor for recurrence. Metastatic tumors have a poor prognosis with no long term survival. Chemotherapy is not active in advanced disease.

Consent: Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests: The authors report no conflicts of interests. The authors alone are responsible for the content and writing of the paper. All authors have contributed to this paper

Authors’ contributions: SK, NB and RA were in charge of the overall care of the patient, reviewed literature, and drafted the manuscript and revised it critically for important intellectual content. HB, MG, MM and IA, carried out the literature review. JK, KS, FK and BE have participated in the histological diagnosis of the case. HM, HE carried out the conception of the case, revised it critically for important intellectual content. All authors read and approved the final manuscript.

Reference


Figures

Fig 1. Chest scan of patient nº 3

Fig 2. Histologic exam of patient nº 3


Survival of breast cancer in very young women <35 years treated in Tripoli/Libya

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Key words: Breast cancer, Young female, Disease Free survival DFS, Overall survival OS.

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Abstract

Study objective: To study survival of breast cancer in very young age women < 35 years over the period between 2000-2005. To relate recurrence rate and survival to risk factors as lymph node involvement, and Estrogen and progesterone status.

Design and setting: Non-randomized retrospective study in patients with breast cancer confirmed by biopsy in Oncology department in TMC.

Patients: 552 patients were seen, 93 patients < 35 years representing 16.8% were included in this study.

Results: Patients < 35 represent 16.8%. Their stages were not different from older patients, No difference in tumor grade. In the majority of the patients under 35 years estrogen and progesterone receptor status were negative (55.6%), but the majority of the patients over 35 years were estrogen and progesterone receptor positive (55.5%) (p=0.035). Visceral metastases were more common in the under 35 years (50%) versus (29%) in patients above 35 years (p=0.04). Overall survival rate in very young age at 1st, 2nd and 5th years was 94.5%, 85% and 74% respectively, while overall survival rate in patients above 35 years at 1st, 2nd and 5th years was 96%, 89% and 81% respectively regardless of age. (p=0.04).

Overall recurrence rate at 1st, 2nd and 5th years and survival rate was better in node negative patients than node positive patients regardless of age (p=0.01). Overall recurrence rate at 1st, 2nd and 5th years and survival rate was better in estrogen positive patients than in estrogen negative patients p=0.04.

Conclusion: women < 35 have a poor prognosis despite a similar stage and grade to older women. They have more estrogen and progesterone negative status tumors (p=0.035) and greater tendency to develop visceral metastases than older women.

Introduction

The prognosis of breast cancer in young women is thought to be worse than older women however this issue is heavily debated. About 2% of patients with breast cancer are <35 years old at diagnosis. (1, 2). Breast cancer at young age tends to be more aggressive and associated with poor prognosis compared with older patients. Tumors in young women were less differentiated, high grade, has high proliferating fraction and had more vascular invasion and negative steroid hormone receptors (3-6). One study concluded that younger patients with ER-positive tumors had a significantly worse prognosis than younger patients with ER negative tumors. (7)

Also they have reduced efficacy of adjuvant chemotherapy for these very young patients with endocrine responsive tumors. (8)

The occurrence of early onset breast cancer has been associated with mutation in BRCA1 and BRCA2 genes. The majority of breast cancer patients found to have BRCA1 and BRCA2 reveal a family history of breast cancer and /or ovarian cancer in at least one first degree relatives. (9-11) Women diagnosed with breast cancer at age of < 35 years are likely to have BRCA1, BRCA2 mutation in up to 15-30%.

These mutations are frequently associated with higher histological grade, lack of estrogen receptors, and high proliferating rate. (12-14)

The age at diagnosis was still a significant predictor with each year younger than 45 years adding 5% to the relative risk of death from breast cancer. (15)

Aims of the study

1-To study Patients characteristics and stage at disease presentation in young < 35 years and older than > 35 years.

2-To study the various predictive and prognostic factors affecting survival (hormone receptor status, and lymph node status and age respectively ) in women younger than 35 years in comparison to older women.

3-To compare between these two groups regarding survival rate at 1st , 2nd , 5th years.

Materials and Methods

552 breast cancer patients who were registered in Oncology clinic in Tripoli Medical Center between Jan. 2000-Dec.2005. The Ethical committee in Tripoli Medical Center approve the study.
Results

552 patients were diagnosed with breast cancer in Tripoli Medical Center in period between 2000-2005 with mean age of 45 years and 56% were premenopausal. 1.8% were male. 93 (16.8%) of patients were less than 35 years. Among these patients <35 years, 17.7% has positive family history of breast cancer in contrast only 14.8% in patients > 35 years had family history of breast cancer (p=0.3). The clinical and pathological characteristic status grouped as group 1 (< 35 years) and group 2 (> 35 years). Table-1.

Tumor size in group 1 tends to be large T3 and T4 (p=0.05), while group 2 have small sized tumor (T1 and T2) (p=0.04).

Both groups have positive lymph node, it was 58% in group 1 and 60.8% in group 2. There were no significant difference in lymph node involvement between these two groups (p=0.189).

Regarding hormone receptors, 55.5% of group 2 patients have positive hormonal receptors while only 44.4% of group 1 patients have positive hormonal receptors. This means younger women tend to have more hormone negative receptor (p=0.035).

Tumor grade was assessed in 38% of patients, there was no statistical difference in tumor grade between two groups (p=0.89).

HER-2 receptor was assessed only in 17.8% of all patients, 33% had strong positive HER-2 receptor by immunohistochemistry study. There was no difference between two groups, 33% in group 1 vs. 30% in group 2.

In group 1, mastectomy and Axillary clearance was done in 75.3%, lumpectomy and Axillary clearance was done in 19.4% and only biopsy was done in 5.4%, in group 2, mastectomy and Axillary clearance was done in 76.6%, lumpectomy and Axillary clearance was done in 15.2% and only biopsy was done in 6.2% (p=0.6).

Adjuvant chemotherapy was given to 86% of group 1, in form of Anthraclyline based chemotherapy in 78.5% of patients and Taxane -Anthraclyline based chemotherapy was given in 7.5% of cases while 82.8% of group 2 received chemotherapy, 70% received CAF (Cyclophosphamide, Adriamycin and 5-flourouricil). 5.4% received CMF (Cyclophosphamide Methotrexate and 5-flourouricil). 7.4% received Taxanes based chemotherapy. (p=0.6).

58% of all patients received adjuvant radiotherapy to chest wall and the axilla that had breast conserving surgery or locally advanced tumors, or more than 3 positive lymph node. Tamoxifen was given to those who are positive estrogen and/or progesterone receptors or unknown receptor status. 50.5% of group 1 received Tamoxifen while it is given to 71.9% of group 2 (p=0.001), because there was more positive receptor status in patients > 35 years. Ovarian ablation was done in 34.3% of group 1. It was done by LHRH analogue in 97% of patients and 3% by radiotherapy.

Higher proportion of patients in group 1 developed visceral metastases 50% as liver, lung, brain) compared with 29% in patients group 2 (p=0.04).

Isolated bone metastases were observed in 25% of patients in group 1 and 28% in patients group 2. 25% of patients group 1 has local recurrence while only 15.6% patients in group 2 developed local recurrence.

There was difference in cumulative recurrence rate in both groups at 1st, 2nd and 5th years. Overall cumulative recurrence rate in patients of group 1 was 10.8%, 22.9% and 32.4% at 1st, 2nd and 5th years versus 13.8%, 23.4% and 36.4% in patients of group 2 at 1st, 2nd and 5th years.

Overall survival rate was better in women more > 35 years at 5 years. Overall survival rate in patients of group 1 are 94.5%, 85%, and 74.3% at 1st, 2nd and 5th years versus 95.4%, 88.8% and 81% in patients of group 2 at 1st, 2nd and 5th years (p=0.01).

Regarding hormone receptors status patients who are estrogen receptor positive had better survival than those with negative hormone receptors p=0.04 fig -1.

In group 1 patients with ER positive receptors, had overall survival at 1st, 2nd and 5th years of 95%, 90% and 85%, while ER negative receptors patients, had overall survival at 1st, 2nd and 5th years 95%, 77%, 73% (p=0.05).

In patients group 2 with ER- positive receptors had overall survival at 1st, 2nd and 5th years of 97%, 89.6% and 82.9%, where ER negative receptors overall survival at 1st, 2nd and 5th years 95%, 83%, 71% (p=0.04).

Patients who were under 35 years and were ER positive had a similar survival to those who were ER positive and over 35 years, 95%, 90% and 85% vs 97%, 89.6% and 82.9%, at 1st, 2nd and 5th years (p=0.82).

Patients who were under 35 years and were ER negative had a similar survival to those who were ER negative and over 35 years, 95%, 77%, 73% vs 95%, 83%, 71%, at 1st, 2nd and 5th years (p=0.46).

Lymph node involvement was a very powerful prognostic of survival in both groups, patients <35 years without nodal involvement had a survival of 100%, 95% and 88.9% at 1st, 2nd and 5th years while those whose lymph node were involved had a survival of 93.6%, 82.1% and 60% at 1st, 2nd and 5th years.

Patients 35 years without nodal involvement had a survival of 100%, 99% and 95% at 1st, 2nd and 5th years while those whose lymph node were involved had a survival of 95.2%, 86% and 77% at 1st, 2nd and 5th years.

The presence of positive lymph node had more adverse effect on survival in group 1 < 35 years than older group 2 > 35 years, 93.6%, 82% and 60% in patients <35 years versus 95%, 86% and 77% at 1st, 2nd and 5th years in patients > 35 years (p=0.014).

Patients who were node negative had similar survival in both groups, 100%, 95%, 88.9% in group 1 vs. 100%, 99%, 95% in group 2 at 1st, 2nd and 5th years (p=0.3) fig -2.

Discussion

Young breast cancer reported to have worse prognosis than older group and some studies shows no difference between two groups, it’s a matter of controversy and still understudy.

Young women below 35 years of age represent less than 2% of the total breast cancer population in Western countries. (1, 2)

In our study 16.8% of patients were below 35 years which is significantly different from other results. In fact it represents the highest recorded percentage reported. 67% of our patients are below 50 years. 56% are premenopausal.

In Colleoni et al study, 4.7% of patients are very young < 35 years, and only 47% are less than 50 years (7).
N. Elsaghir et al study, only 8.1% of patients are < 35 years old, 53% are < 50 years, and 44% are premenopausal (16). In Korean study, 14.6% of patients are less than 35 years (18).

Young patients have poor prognostic factor than older group, they have more bigger tumor size as T3 and T4 and more negative hormone receptor which is similar to other studies Colleoni, El saghir, Elisabetta study, the Korean study and A Chan et al. (7, 16, 17, 18, 19, 20). Regarding lymph node involvement, it was no difference between the two groups, which is similar to Colleoni (7) and Alsaghir (13) studies, but Korean study shows more lymph node positive involvement in young patients (P<0.024) (18,19).

In our study patients who are less than 35 years have poor survival and more visceral metastases than patients who are more than 35 years. In our study, Patients who have positive estrogen receptors have better survival than those with negative receptor tumor in both groups, and there was no difference in survival between patients who are less than 35 years and more 35 years if they were Estrogen positive or negative.

In Elsaghir study, it shows poor survival in positive receptors in young women than old women but not in negative receptors status (16).

In Colleoni et al, younger patients with Estrogen positive tumors had significantly worse prognosis than old women (7).

In Elisabetta et al study shows that five year survival was not different in the three groups 91%, 90%, and 89% for very young, young and old age respectively.

In our study, patients less than 35 years who had positive lymph node had worse survival (p=0.014) than patients more than 35 years, but no effect on survival if it was negative lymph node, which shows similar results to Elsaghir study (16).

Tumor grade and vascular invasion has negative impact on survival in patients who are less than 35 years which was not studied in our patients because of small number of patients (7). In some studies, among young and older breast cancer patients treated, outcome measures were similar in both groups of women. There was no significant difference in tumor characteristic, local disease relapse and distant metastases in both groups. (21)

**Conclusion**

Women less than thirty five years have a poor prognosis despite a similar stage and grade to older women. These women have more estrogen and progesterone negative status tumors (p=0.035), and have greater tendency to develop visceral metastases than older women.

Patients who have positive estrogen receptors have better survival than negative receptors in both groups. No difference in survival between patients who are less than 35 years and those older than 35 years if they had similar hormone receptor status. Patients less than 35 years who had positive lymph node had worse survival than patients more than 35 years, but no effect on survival if it was negative lymph node. (p=0.014), but those patients with negative lymph nodes have similar survival to older patients with negative lymph nodes.

**Tables**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1</th>
<th>Group 2</th>
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<tr>
<td>Age</td>
<td></td>
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<tr>
<td>1&lt; 35 years</td>
<td>93</td>
<td>459</td>
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<td>2-Tumor Size</td>
<td></td>
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<tr>
<td>T1+T2</td>
<td>31(33%)</td>
<td>199(43%)</td>
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<tr>
<td>T3+T4</td>
<td>47(50%)</td>
<td>186(40%)</td>
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<tr>
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<td>54(58%)</td>
<td>279(60.8%)</td>
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<td>22(23.6%)</td>
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<td>4-Stage</td>
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<td></td>
<td></td>
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<tr>
<td>I</td>
<td>2(2%)</td>
<td>15(3.3%)</td>
<td>0.57</td>
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<tr>
<td>II</td>
<td>34(36.6%)</td>
<td>203(44.2%)</td>
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<tr>
<td>III</td>
<td>37(39.8%)</td>
<td>150(32.7%)</td>
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<td>47(10.2%)</td>
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<td>Ductal(IDC)</td>
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<td>31(33%)</td>
<td>183(39.9%)</td>
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<tr>
<td>Negative</td>
<td>6(6%)</td>
<td>11(6%)</td>
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<td>Lobular(ILC)</td>
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<td>12(6%)</td>
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<tr>
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<td>Positive</td>
<td>2(2.2%)</td>
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<td>Mixed ILC+IDC</td>
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<tr>
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<td>5(5.4%)</td>
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<td>31(33.3%)</td>
<td>183(39.9%)</td>
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<td>6-Grade(known)</td>
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<td>11(35.5%)</td>
<td>68(37.2%)</td>
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<td>E.R</td>
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<tr>
<td>Positive</td>
<td>28(44.4%)</td>
<td>166(55.9%)</td>
<td>0.035*</td>
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<tr>
<td>Negative</td>
<td>35(55.6%)</td>
<td>131(44.1%)</td>
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<tr>
<td>PR</td>
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<tr>
<td>Positive</td>
<td>29(46%)</td>
<td>175(58.9%)</td>
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<tr>
<td>Negative</td>
<td>34(53.9%)</td>
<td>122(41.1%)</td>
<td>0.03*</td>
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<td>8-Recurrence</td>
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<tr>
<td>Visceral</td>
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<td></td>
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<tr>
<td>Positive</td>
<td>12(24%)</td>
<td>39(134(29%)</td>
<td>0.044*</td>
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<tr>
<td>Bone</td>
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<tr>
<td>6(24%)</td>
<td>38(134(37.9%)</td>
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<tr>
<td>Local</td>
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<tr>
<td>6(24%)</td>
<td>21(134(15.6%)</td>
<td></td>
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<tr>
<td>9-Overall</td>
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<tr>
<td>1&lt; year</td>
<td>9(6%)</td>
<td>13(8%)</td>
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<td>2&lt; year</td>
<td>22(9%)</td>
<td>23(4%)</td>
<td>0.941</td>
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<tr>
<td>5&lt; year</td>
<td>44(4.4%)</td>
<td>36(4%)</td>
<td>0.514</td>
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<tr>
<td>Survival</td>
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<tr>
<td>1&lt; Year</td>
<td>95%</td>
<td>96%</td>
<td>0.01</td>
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<tr>
<td>2&lt; Year</td>
<td>86.5%</td>
<td>90%</td>
<td></td>
</tr>
<tr>
<td>5&lt; Year</td>
<td>68.5%</td>
<td>81.4%</td>
<td></td>
</tr>
</tbody>
</table>
Figures

Fig 1. Overall survival in hormone positive and negative in both groups 1 and 2.

Fig 2. Overall survival in Lymph node positive and negative in both groups 1 and 2.

References

Bilateral Breast Cancer- A case Report

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Abstract

Introduction: Breast cancer is one of the most important health problems in the world and affects a great number of women over the entire globe. This group of tumors rarely presents as bilateral disease and, when it does happen, normally occurs within the same biological type. We report a case of concurrent bilateral breast cancer with two different biological types, ER, PR is positive in left breast and were negative in right breast, in a 58 –year old women referred to our oncology center.

Case presentation:
A 58 –year old woman referred to our oncology center in November 2012, presented with right breast mass of 7.0× 5.0 cm and left breast mass of 2×2cm. Biopsy had received invasive duct carcinoma G III with ER, PR positive and Her-2negative in left Brest, and invasive duct carcinoma G II with ER, PR negative and Her-2negative in right breast. She was submitted for neoadjuvant chemotherapy 4 cycles of AC followed by bilateral modified radical mastectomy then adjuvant 4 cycles of docetaxel followed by radiotherapy of the thoracic wall and axillary nodes. Hormonal receptors were positive in the tumor of left breast so she started letrozole.

Conclusion: The risk of development of bilateral breast cancer is about 1%each year within similar histological and biological types. In this case, the biological types are different, which is not common.

Introduction
Breast cancer is one of the most important health problems in the world. The American Cancer Society estimates that 234,580 Americans will be diagnosed with breast cancer and 40,030 will die of the disease in the United States in 2013(1). The incidence of breast cancer has increased steadily over the past few decades, but the breast cancer mortality appears to be declining, suggesting the benefit from early detection and more effective treatment(2). Many risk factors are associated with the occurrence of breast cancer (6). We report a case of concurrent breast cancer with the same histological type but with different biological types.

Case presentation
A 58 –year old woman, a housewife from El-Taif, noticed a mass in right breast, and in January 2013, she was sent by King Abdul-Aziz doctors to King Abdullah Medical City Oncology Center with right breast mass of 7.0× 5.0 cm in upper outer quadrant and supraareolar area, firm to hard in consistence, irregular border and thickened mobile overlying skin with freely mobile right axillary lymph node about 2×2 cm; also there was left breast mass of 2×2cm retroareolar with no palpable axillary lymph nodes. She was a postmenopausal patient with gynecological histories of 3 pregnancies; the first when she was 21 years old, and no abortion history was noted. She denied the use of an oral contraceptive pills, and she had no relevant family history.

Bilateral mammography and Ultrasound revealed» large irregular  speculated ill-defined margins, heterogeneous hyper dense right breast mass approximately 5.7 × 3.6 cm approximately opposite 11 o clock with multiple highly suspicious right axillary lymph nodes were noted, the largest measures approximately 1.8× 1.3 cm with overlying skin thickness. Small (0.8 cm × 0.6cm) opacities and multiple scattered and clustered micro calcifications are noted at retroareolar area of left breast approximately opposite 6 o clock position. Right axillary lymph node enlargement was noted.

Needle biopsy was taken and showed:
1- Right breast, invasive duct carcinoma, grade III, estrogen receptor(ER) 0%, progesterone receptor (PR) 0% with Her-2/neu negative (score 0).
2-Left breast, invasive duct carcinoma, grade II, estrogen receptor (ER) 90%, progesterone receptor (PR) 70% with Her-2/neu negative (score 1). (Figure 1a, b, c, d)
This patient was diagnosed as stage IIIB right breast cancer (T3N2 M0) and stage I left breast cancer (T1N0M0). She was submitted for neoadjuvant chemotherapy 4 cycles of AC (Adriamycin 60mg/m² & cyclophosphamide 600mg/2) followed by bilateral modified radical mastectomy, with pathological surgical report showed that:

1- Right breast, invasive duct carcinoma NOS, grade III, T 5cm, DCIS present, high nuclear grade, - ve SM, LVI is present and one out of 20 lymph nodes is positive for metastasis (1/20). Estrogen receptor (ER) 0%, progesterone receptor (PR) 0% with Her-2/neu negative (score 0); Triple negative.

2- Left breast: no residual tumor only fibrocystic changes and all lymph nodes were negative for metastasis (0/12). Estrogen receptor (ER) 90%, progesterone receptor (PR) 70% with Her-2/neu negative (score 1). (Figure 2)

This patient was diagnosed as stage IIIB right breast cancer (T3N2 M0) and stage I left breast cancer (T1N0M0). She was submitted for neoadjuvant chemotherapy 4 cycles of AC (Adriamycin 60mg/m² & cyclophosphamide 600mg/2) followed by bilateral modified radical mastectomy, with pathological surgical report showed that:

1- Right breast, invasive duct carcinoma NOS, grade III, T 5cm, DCIS present, high nuclear grade, - ve SM, LVI is present and one out of 20 lymph nodes is positive for metastasis (1/20).

Estrogen receptor (ER) 0%, progesterone receptor (PR) 0% with Her-2/neu negative (score 0); Triple negative.

2- Left breast: no residual tumor only fibrocystic changes and all lymph nodes were negative for metastasis (0/12). Estrogen receptor (ER) 90%, progesterone receptor (PR) 70% with Her-2/neu negative (score 1). (Figure 2)

Then received adjuvant therapy in the form of 4 cycles of docetaxel (80 mg/m²) then Radiotherapy 50 Gy (2 Gy dose daily, five weekly fractions) to thoracic wall and axillary nodes of right breast. Hormonal receptors were positive in the tumor of left breast so adjuvant hormonal therapy with letrozole 2.5mg was prescribed.

Discussion

Bilateral breast cancer is uncommon finding and is reported to account for only 2% of women with breast cancer. The risk factors associated with bilateral occurrence are: familial or hereditary breast cancer, young age at primary breast cancer diagnosis, lobular invasive carcinoma, multicentricity and radiation exposure (6, 7). Contra lateral breast cancer is either a metastatic lesion or the second primary cancer, and occurs either synchronously or metachronously. Chaudary et al. (8) categorized contra lateral breast cancer into a metastatic lesion or second primary cancer based only on pathologic criteria. Several reports showed that the prognosis in bilateral breast cancer was worse than that of unilateral breast cancer (9, 10). There have also been many debates regarding biological and therapeutic aspects of bilateral breast cancers (11, 12). Considering these points, it is important to know whether contra laterals breast cancer is a metastatic lesion or the second primary cancer.

Such type of patients is lower disease free survival and higher rates of distance metastasis are a recognized feature of bilateral breast cancer which therefore has worse overall survival compared to unilateral tumors (13). Our patient treated in curative intent in the form of neoadjuvant chemotherapy then bilateral modified radical mastectomy followed by radiotherapy then adjuvant hormonal treatment, and need close follow up due to high incidence of recurrence.

Conclusion

In conclusion we note that in women, who present with bilateral breast cancer should be investigated for distance metastasis at presentation even in whose who are asymptomatic. Only few cases have been reported in the literature. Further study is recommended.

References


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Mission

Fight Cancer on all fronts through all possible direct and indirect channels & by all means.

Activities

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<tr>
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<th>ACTIVITIES</th>
<th>LOCATION</th>
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<tr>
<td>February 4, 2013</td>
<td>Lung Cancer Symposium “International Cancer Day”</td>
<td>Sheraton Hotel, Dammam</td>
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<td>February 6, 2013</td>
<td>Breast Cancer Symposium for Primary care physicians</td>
<td>Bisha</td>
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<tr>
<td>February 27-28, 2013</td>
<td>Updates on Multiple Myeloma Symposium</td>
<td>Sheraton Hotel, Dammam</td>
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<td>March 13, 2013</td>
<td>1 day Mini Symposium “Updates in Colorectal Cancer” (International Colorectal Cancer Month)</td>
<td>Sheraton Hotel, Dammam</td>
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<td>March 21, 2013</td>
<td>Breast Cancer Symposium for Primary care physicians</td>
<td>Madinah</td>
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<tr>
<td>April 3 &amp; 4, 2013</td>
<td>ASCO – GFFCC Conference Hepatobiliary Pancreatic Cancer Conference</td>
<td>King Fahd Medical City, Riyadh</td>
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<tr>
<td>April 02, 2013</td>
<td>Breast Cancer Symposium for Primary care physicians</td>
<td>Jeddah</td>
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<tr>
<td>April 18, 2013</td>
<td>Breast Cancer Symposium for Primary care physicians</td>
<td>Makkah</td>
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<tr>
<td>April 25, 2013</td>
<td>Pharmacology Oncology Symposium</td>
<td>Sheraton Hotel, Dammam</td>
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<tr>
<td>May 8, 2013</td>
<td>Advanced Management of Breast Cancer</td>
<td>Plaza Conference Center, Aramco</td>
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<td>September 15, 2013</td>
<td>Latest Improvement of Lymphoma Management (International Lymphoma Day)</td>
<td>Plaza Conference Center, Aramco</td>
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<td>October 2013</td>
<td>“5th Sharqiyah Wardiyah” Breast Cancer Campaign</td>
<td>Eastern Province</td>
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<tr>
<td>November 20, 2013</td>
<td>Sick Children’s Day</td>
<td>Sunset Beach Resort</td>
</tr>
</tbody>
</table>
REGISTRATION IS NOW OPEN

Call for abstracts

Tawam Hospital

Emirates Oncology Conference 2013

November 14-15-16 2013, Emirates Palace, Abu Dhabi, UAE

In Collaboration with MENA-NCCN Regional Meeting

This event is recommended by EASO

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Jihad Kanbar, T: 00971-3-7074742 - F: 00971-3-7074837
email: jkanbar@tawamhospital.ae

For Registration visit conference website: www.emiratesoncology.ae

Working towards applying for CME accreditation

Faculty of Medicine and Health Sciences

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Informations :

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<table>
<thead>
<tr>
<th>MONTH</th>
<th>Event</th>
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<tbody>
<tr>
<td>JANUARY</td>
<td>Cervical Cancer Awareness Month</td>
</tr>
<tr>
<td>FEBRUARY</td>
<td>Screening and Early Detection Awareness Month</td>
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<tr>
<td>MARCH</td>
<td>Colorectal Cancer Awareness Month</td>
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<tr>
<td>APRIL</td>
<td>Cancer Fatigue Awareness Month</td>
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<tr>
<td>MAY</td>
<td>Melanoma and Skin Cancer Awareness Month</td>
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<td>JUNE</td>
<td>National Cancer Survivors Day</td>
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<td>JULY</td>
<td>Sarcoma Awareness Month</td>
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<tr>
<td>AUGUST</td>
<td>Pain Medicine and Palliative Care</td>
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<tr>
<td>SEPTEMBER</td>
<td>Gynecologic Cancer Awareness Month</td>
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<td>Prostate Cancer Awareness Month</td>
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<td>Leukemia and Lymphoma Awareness Month</td>
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<tr>
<td>OCTOBER</td>
<td>Breast Cancer Awareness Month</td>
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<tr>
<td>NOVEMBER</td>
<td>Lung Cancer Awareness Month</td>
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<td></td>
<td>Smoking Cessation</td>
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<tr>
<td>DECEMBER</td>
<td>5 A Day Awareness Month</td>
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Objectives & Scope Of The PAJO

The Pan Arab Journal of Oncology (PAJO) is the official Journal of the Arab Medical Association Against Cancer (AMAAC). It is a quarterly publication targeting health professionals interested in the oncology field. It is a multidisciplinary peer-reviewed journal that publishes articles addressing medical oncology, malignant hematology, surgery, radiotherapy, pediatric oncology, geriatric oncology, basic research and the comprehensive management of patients with malignant diseases in addition to international oncology activities, congresses & news.

The journal will be addressed, as a first step, mainly to the professionals in the hematology & oncology field in the Middle East region and North Africa. The goal is to share local & regional research activities news and to be updated with international activities. We hope, with your support, to achieve our following objectives:

1. Promote and encourage research activities in the Arab World.
2. Disseminate & analyze epidemiological local, regional and international data.
3. Update health professionals with the most recent advances, news & developments in the field of oncology.
4. Improve the level of scientific publications arising form the Arab World.
5. Keep health professionals connected and exposed to the activities of different Arab cancer societies.
6. Share with our immigrant compatriots their activities & feedback in this field.
7. Involve all health professionals interested in the field of Oncology within the multidisciplinary scope of the Journal.
8. Encourage post graduates students to submit their research work.

Instructions For The Authors

1. Manuscript Categories

1.1. Clinical trials
The Editor-in-Chief and an Associate Editor generally review Reports from clinical trials. Selected manuscripts are also reviewed by at least two external peer reviewers. Comments offered by reviewers are returned to the author(s) for consideration. Manuscript acceptance is based on many factors, including the importance of the research to the field of oncology & the quality of the study. Authors should focus on accuracy, clarity, and brevity in their presentation, and should avoid lengthy introductions, repetition of data from tables and figures in the text, and unfocused discussions. Extended patient demographic data should be included in a table, not listed within the text. Reports from Clinical trials are limited to 3,000 words of body text, excluding the abstract, references, figures, and tables. They are limited to six total figures and tables. All abstracts are strictly limited to 250 words. Titles are to be descriptive, but succinct. Results of clinical studies should be supported by a clear description of the study design, conduct, and analysis methods used to obtain the results. Reports of phase II & III studies should include from the protocol a clear definition of the primary end point, the hypothesized value of the primary end point that justified the planned sample size, and a discussion of possible weaknesses, such as comparison to historical controls. Phase I studies will be well received if they have interesting clinical responses, unusual toxicity that pointed to mechanism of action of the agents, and important or novel correlative laboratory studies associated with the trials.

1.2. Review Articles
All reviews must be clinically oriented, ie, at least half the review must describe studies that detail human impact, marker effect on prognosis, or clinical trials. Review Articles should be prepared in accordance with the Journal’s Manuscript Preparation Guidelines, and will be reviewed in the same manner as Reports from Clinical Trials. Reviews are limited to 4,500 words of body text, excluding the abstract, references, figures, and tables. The editors also suggest a limit of 150 references.

1.3. Editorials / Comments / Controversies
The Editor-in-Chief may solicit an Editorial to accompany an accepted manuscript. Authors who wish to submit unsolicited Comments and Controversies should contact the Editor-in-Chief, before submission to determine the appropriateness of the topic for publication in the Journal. Editorials should be no more than four to five pages in length.

1.4. Articles on Health Economics
Articles about health economics (cost of disease, cost-effectiveness of drugs, etc) are highly encouraged.

1.5. Case Reports / Correspondence / Special Articles
Correspondence (letters to the Editor) may be in response to a published article, or a short, free-standing piece expressing an opinion, describing a unique case, or reporting an observation that would not qualify as an Original Report. If the Correspondence is in response to a published article, the Editor-in-Chief may choose to invite the article’s authors to write a Correspondence reply. Correspondence should be no longer than three pages in length. Special Articles present reports, news from international, regional societies as well as news from our compatriots.
2. Manuscript submission procedure

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3. Disclosures of Potential Conflicts of interest

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4. Manuscript Preparation Guidelines

Title Page
The first page of the manuscript must contain the following information: (1) title of the report, as succinct as possible; (2) author list of no more than 20 names (first name, last name); (3) names of the authors’ institutions and an indication of each author’s affiliation; (4) acknowledgments of research support; (5) name, address, telephone and fax numbers, and e-mail address of the corresponding author; (6) running head of no more than 80 characters (including spaces); (7) list of where and when the study has been presented in part elsewhere, if applicable; and (8) disclaimers, if any.

Abstract
Abstracts are limited to 250 words and must appear after the title page. Abstracts must be formatted according to the following headings: (1) Purpose, (2) Patients and methods (or materials and methods, similar heading), (3) Results, and (4) Conclusion. Authors may use design instead of Patients and methods in abstracts of Review Articles. Comments and Controversies, Editorials and Correspondence do not require abstracts.

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Reference Style

- Journal article with one, two, or three authors

- Journal article with more than three authors

- Journal article in press (manuscript has been accepted for publication)

- Supplement
results and prognostic factors among 138 patients with advanced Hodgkin’s disease treated with the alternating MOPP/ABVD chemotherapy. Ann Oncol 5:S53-S57, 1994 (suppl 2)

1. Book with a single author

3. Book with multiple authors

5. Chapter in a multiauthored book with editors

7. Abstract

10. Conference/meeting presentation

12. Internet resource

14. Digital Object Identifier (DOI)

16. Government Announcement/Publication

18. ASCO Educational Book

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