

Clinical characteristics and relapse experiences of Albanian women diagnosed with breast cancer and treated with Anthracycline-based regimens as adjuvant chemotherapy

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Abstract

Aim: The aim of this study was to assess the distribution and clinical characteristics of women diagnosed with breast cancer and treated with anthracycline-based regimens, CAF or AC-CMF, as adjuvant chemotherapy in Albania.

Methods: A case-series study was conducted at the University Hospital Center "Mother Teresa" in Tirana during the period 2005-2007 including 146 women diagnosed with breast cancer and treated with adjuvant chemotherapy. The clinical diagnosis was based on the biopsy findings. Subsequently, all women were followed-up during the period 2010-2012. The relapse experience was recorded for all women included in the study. Fisher's exact test was used to compare the distribution of demographic and clinical characteristics of women according to their relapse status at the end of the follow-up period.

Results: There were 142 (97.3%) women treated with CAF and 4 (2.7%) women treated with AC-CMF. Overall, 34 (24.5%) women experienced relapse within four years compared with 105 (75.5%) women who did not manifest relapses after the fourth year of follow-up. The proportion of at least three positive nodules was considerably higher among women who experienced relapse compared with their counterparts who did not experience relapse (54.5% vs. 25.9%, respectively, $P=0.036$). Conversely, there were no significant differences regarding the age-group, cancer type, or hormonal values of women.

Conclusion: Our study provides useful evidence about the distribution and clinical characteristics of Albanian women treated with CAF or AC-CMF.

Keywords: AC-CMF, CAF, cancer, chemotherapy.

Introduction

Approximately, 600 new cases of breast cancer are diagnosed annually in Albania, which is the second most frequent cancer after lung cancer. Cancer mortality constitutes the second cause of death in Albania following deaths from circulatory system diseases (1). The treatment of breast cancer generally involves multiple modalities including surgery, radiation and/or chemotherapy. *Adjuvant treatment* is the administration of additional therapy after primary surgery to kill or inhibit micrometastasis (2). Depending on the model of risk reduction, adjuvant therapy has been estimated to be responsible for 35%-72% of the reduction in mortality rate (3).

Anthracyclines, one of the first chemotherapeutic agents introduced in the 1960s, has been the backbone in the treatment of breast cancer for the last 30 years and has been used extensively. By the 1980s, anthracycline-based combination regimens established themselves as a primary class of chemotherapy regimens used in the treatment of early and advanced stages of breast cancer (4).

In Albania, the anthracycline-based regimens are the main adjuvant chemotherapy for breast cancer treatment, due to limited hospital budget for this purpose. Hence, there is a need to understand better the benefit from this family of drugs in terms of relapse episodes and to identify the clinical characteristics which are important in increasing the relapse rate.

In this framework, the aim of this study was to assess the distribution and clinical characteristics of women diagnosed with breast cancer and treated with anthracycline-based regimens, CAF or AC-

CMF, as adjuvant chemotherapy in Albania.

Methods

A case-series study was conducted at the University Hospital Center "Mother Teresa" in Tirana during the period 2005-2007 including 146 women diagnosed with breast cancer.

The clinical diagnosis was based on the biopsy findings. Subsequently, all women were followed-up during the period 2010-2012. The relapse experience was recorded for all women included in the study. Fisher's exact test was used to compare the distribution of demographic and clinical characteristics of women according to their relapse status (relapse vs. no relapse at the end of the follow-up period). In all cases, a p-value ≤ 0.05 was considered as statistically significant. The Statistical Package for Social Sciences (SPSS, version 17.0) was used for all the statistical analyses.

Results

Overall, there were 146 women treated with CAF (N=142, or 97.3%) or AC-CMF (N=4, or 2.7%). Table 1 presents the distribution of relapse time among women treated with CAF or AC-CMF. There were seven women with missing data on the relapse time and, therefore, this analysis consisted of 139 women. On the whole, 6 (4.3%) women experienced a relapse within the first 12 months; 13 (9.4%) within 24 months; 6 (4.3%) within 36 months; and 9 (6.5%) women within 48 months. On the other hand, 105 (75.5%) did not manifest relapses after the fourth year of follow-up.

Table 1. Distribution of relapse time among women treated with CAF or AC-CMF

Relapse time	Number	Percentage
<12 months	6	4.3
12-24 months	13	9.4
25-36 months	6	4.3
37-48 months	9	6.5
>49 months	105	75.5
<i>Total</i>	<i>139</i>	<i>100.0</i>

Table 2 displays the distribution of demographic and clinical characteristics by relapse episodes of women. For this analysis, women were dichotomized into: “no relapse at all” (104 women who did not experience relapse after the fourth year of follow-up) vs. “relapse” (34 women, regardless of the time period of their relapse).

Women who experienced relapse were generally younger than those who did not manifest relapse at the end of the follow-up period (the proportion of women aged 56-70 years was 17.6% vs. 30.5%, respectively), notwithstanding the lack of statistical significance of this finding (overall $P=0.084$).

There was a higher proportion of ductal cancer types

in women who experienced relapse (67.6%) compared to women who did not experience relapse (50.5%) and this finding was borderline statistically significant ($P=0.062$).

The proportion of at least three positive nodules was considerably higher among women who experienced relapse (54.5%) compared with their counterparts who did not experience relapse (25.9%) and this difference was statistically significant ($P=0.036$).

Conversely, there was no statistically significant difference in the proportions of hormonal values between the two groups (relapse vs. no relapse) [$P=0.203$, Table 3].

Table 2. Distribution of demographic and clinical characteristics by relapse status

Variable	No relapse (N=105)	Relapse (N=34)	P-value [†]
Age-group:			
≤35 years	4 (3.8)*	4 (11.8)	0.084
36-45 years	23 (21.9)	12 (35.3)	
46-55 years	46 (43.8)	12 (35.3)	
56-70 years	32 (30.5)	6 (17.6)	
Cancer type:			
Ductal	52 (50.5)	23 (67.6)	0.062
Lobular	39 (37.9)	11 (32.4)	
Other	12 (11.7)	-	
Nodules:			
Positive 1-3	35 (41.2)	6 (27.3)	0.036
Positive >3	22 (25.9)	12 (54.5)	
Negative	28 (32.9)	4 (18.2)	
Hormonal values:			
Estrogen-Progesterone negative (HER-2 unknown)	18 (18.9)	7 (25.9)	0.203
Estrogen-Progesterone positive (HER-2 unknown)	55 (57.9)	13 (48.1)	
Estrogen-Progesterone positive (HER-2 negative)	16 (16.8)	2 (7.4)	
Estrogen-Progesterone positive (HER-2 positive)	4 (4.2)	4 (14.8)	
Triple negative	2 (2.1)	1 (3.7)	

* Number and column percentages (in parenthesis).

† P-values from Fisher's exact test.

Among women who experienced relapse (N=34), there were 10 (29.4%) cases where the relapse

site involved the lungs; 8 (23.5%) cases with liver involvement; 6 (17.6%) cases with bone invol-

Table 3. Distribution of relapse sites among women who experienced relapse (N=34)

Relapse Time	Number	Percentage
Lungs	10	29.4
Liver	8	23.5
Bones	6	17.6
Other sites	10	29.5
Total	34	100.0

vement; and 10 (29.5%) cases which involved other sites (Table 3).

Discussion

Adjuvant chemotherapy has been estimated to be responsible for 35%-72% of the reduction in mortality rate. Studies conducted in the last few decades have consistently shown that chemotherapy leads to a significantly higher disease-free rate and overall survival in breast cancer patients (5).

The National Surgical Adjuvant Breast and Bowel Project (NASBP) trial was another direct comparison of an anthracycline to a non-anthracycline containing regimen. The anthracycline containing regimen demonstrated a relapse-free survival (RFS) (87% at 5 years) (6). In our study, 75.5% of women demonstrated a relapse-free survival after the fourth year of follow-up.

Multiple components determine the necessity for patients requiring adjuvant chemotherapy. These include, but are not limited to, the tumor size, molecular subtype, histology and its grade. The axillary and regional lymph node status and the tumor hormone receptor expression are also important considerations (7). Nodal status also plays a role with any nodal involvement lowering the survival rate at five years (8). Our study is compatible with this evidence, revealing that the proportion of at least three positive nodules

was considerably higher among women who experienced relapse compared with their counterparts who did not experience relapse (54.5% vs. 25.9%, respectively, $P=0.036$).

According to some studies published in the international literature, breast cancer in young women is more aggressive (9). In our study, there was no significant difference regarding the age-group of women, but it was obvious that women who experienced relapse were generally younger than those who did not manifest relapse at the end of the follow-up.

The most frequent site of relapse in our study involved the lungs, followed by the liver, and next by the bones. The other sites (including the skin, brain, or lymphnodes) altogether represented approximately the same frequency as the first most frequent site (that is the lungs). Determination of the cancer site is important since in order to evaluate the survival rate after recurrence of the disease (10).

In conclusion, our study provides useful evidence about the distribution and clinical characteristics of Albanian women treated with anthracycline-based regimen as adjuvant chemotherapy. The information collected may help to determine the clinical characteristics which affect the recurrence of breast cancer in Albanian women.

Conflicts of interest: None declared.

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