



# Oophorectomy as a Hormonal Ablation Therapy in Metastatic and Recurrent Breast Cancer: Current Indications and Results

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## Abstract

Breast cancer is the commonest malignancy affecting females. Hormone-positive cancers carry a better prognosis. Many adjuvant and palliative endocrine therapies are in use, including surgical ablation. We retrospectively studied seventy-four patients who did bilateral salpingo-oophorectomy (BSO)/bilateral oophorectomy (BO) for factors affecting survival and prognosis. BSO was superior in overall and progression-free survival. Incidental ovarian metastasis carried a grave prognosis. Surgical hormonal ablation is a viable option with laparoscopic BSO as the approach of choice.

**Keywords** Breast cancer · Metastasis · Hormone therapy · Palliation · Oophorectomy

## Background

Breast cancer is the commonest malignancy affecting women in Egypt, as long as, in many other countries throughout the world with estimated annual loads of about 19,000 new cases in 2015 among Egyptian women [1]. Metastasis occur in about 20–30% of cases after surgical treatment of the primary tumour [2].

In a study of the hormonal profile of Egyptian breast cancer patients, Hussein et al. found that about 67% were ER and/or PR positive (luminal types) [3].

Hormonal therapy solely or in combination with chemotherapy as an adjuvant/palliative treatment of luminal type

breast cancer is well established with clinical response in 40–60% of cases, although 10% of patients with hormone-negative breast cancer may also show response [4]. Many hormonal lines are in use as SERMs (for example, tamoxifen), aromatase inhibitors, GnRh agonists/antagonists, fulvestrant, and radiation/surgical ovarian ablation [5]. More recently, the SOFT trial showed that ovarian function suppression in premenopausal breast cancer women did not show a significant benefit in comparison with tamoxifen alone, except in a subgroup of high risk patients who are candidates for neoadjuvant/adjuvant chemotherapy [6].

At the end of the nineteenth century, bilateral oophorectomy procedure was first proposed by Schinzingler as a treatment option for breast cancer, and then, Beatson was the first to perform in a case that was in the luteal phase of her menstrual cycle. Later, Boyd used the procedure as an adjuvant treatment and then championed as an effective endocrine therapy by itself [7].

Since then, many studies were done to assess the role of this therapy in hormonal ablation, its value, case selection and its use as first/second/third-line therapy. However, no conclusive results were obtained and the fact that most studies, as well as this study, were retrospective.

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## Patients and Methods

This a retrospective study in which the hospital electronic archive was searched by both diagnoses of malignant neoplasm of breast and operation of oophorectomy/salpingo-

oophorectomy. Patients were included if they underwent surgical hormonal ablation, histological examination proved breast carcinoma, and receptor status (ER) was confirmed positive. Patients were excluded if they did not have adequate data registered in the hospital archiving system. Seventy-four cases were found fulfilling the research criteria.

The aim of this study is to highlight our experience with surgical ovarian ablation, compare two approaches to achieving surgical ablation, namely, bilateral oophorectomy and bilateral salpingo-oophorectomy, and identify the incidence and value of accidentally detected ovarian malignancy.

The primary endpoint of this study is the overall and progression-free survival.

The data of these patients were analysed, and statistical values were obtained using SPSS version 22 (Inc., Chicago, IL). Continuous variables are presented as mean when symmetrical or median and range when asymmetrical. Categorical variables are presented as proportions. Bivariate analysis was done using the chi-square test. Survival analysis was done using the Kaplan–Meier curve and significance determined by log-rank test.  $p$  value < 0.05 was considered significant.

## Results

The mean age of the patients at the time of the ablative surgery was 39.2 years old (SD approximately 5.8). Infiltrating duct carcinoma (IDC) not otherwise specified represents about 92% of the cases. Thirty-three patients were luminal B, while thirty-two were luminal A type. In most of them (63.5%), the original tumour was grade II. Distant metastasis occurred in multiple sites in 27 cases, visceral metastasis in 10 cases, bone and soft tissue only in 17 cases, while no metastasis in 9 cases (Fig. 1). Patients without metastatic disease were operated due to loco-regional disease progression on other hormonal therapy lines. About 60% of patients were treated primarily by mastectomy, while breast conserving surgery (BCS) and no breast surgery represent 19% each.

Surgical ablation represented first-line endocrine therapy in about 22% of the patients (with almost all the rest starting with tamoxifen), as second-line therapy in about 58% (with AIs the commonest followed by GnRh agonist/antagonist in the remaining cases), and as third line in 16% of cases. The surgical ablation in 51% was through bilateral oophorectomy (BO), while in 49% through bilateral salpingo-oophorectomy (BSO) (actually one case did side SO and side oophorectomy due to difficulty). In 68 out of 74 patients, the operation was done laparoscopically with no reported complications. In 11

patients (about 15%), metastasis was found in pathologic examination of the ovarian tissue, in only 3 of whom the preoperative radiology revealed an ovarian suspicious lesion; however, in the rest, the diagnosis was a pathologic surprise. Nine patients (12.2%) died and 19 cases (25.7%) progressed through the course of follow-up.

The overall estimated mean survival (OS) was about 34.9 months (with standard error 2.3). The OS was significantly better for the BSO group (about 41 months) in comparison with the BO group (26 months) ( $p$  value = 0.005) (Fig. 2). Also, OS of laparoscopy was better, but insignificant. The presence of ovarian metastasis in the specimen carried a worse OS (mean 19 months) although insignificant statistically. The estimated mean progression-free survival (PFS) after the operation was approximately 27.7 months (standard error 2.8). PFS was longer in luminal A (estimated about 23 months versus about 16 months) although non-significant. PFS was also longer in the BSO group, but non-significant (29 and 20 months, respectively) (Fig. 3). PFS for those without malignant deposits in the ovary was significantly longer 29 months, in contrast to 8 months ( $p$  value = 0.005) (Fig. 4).

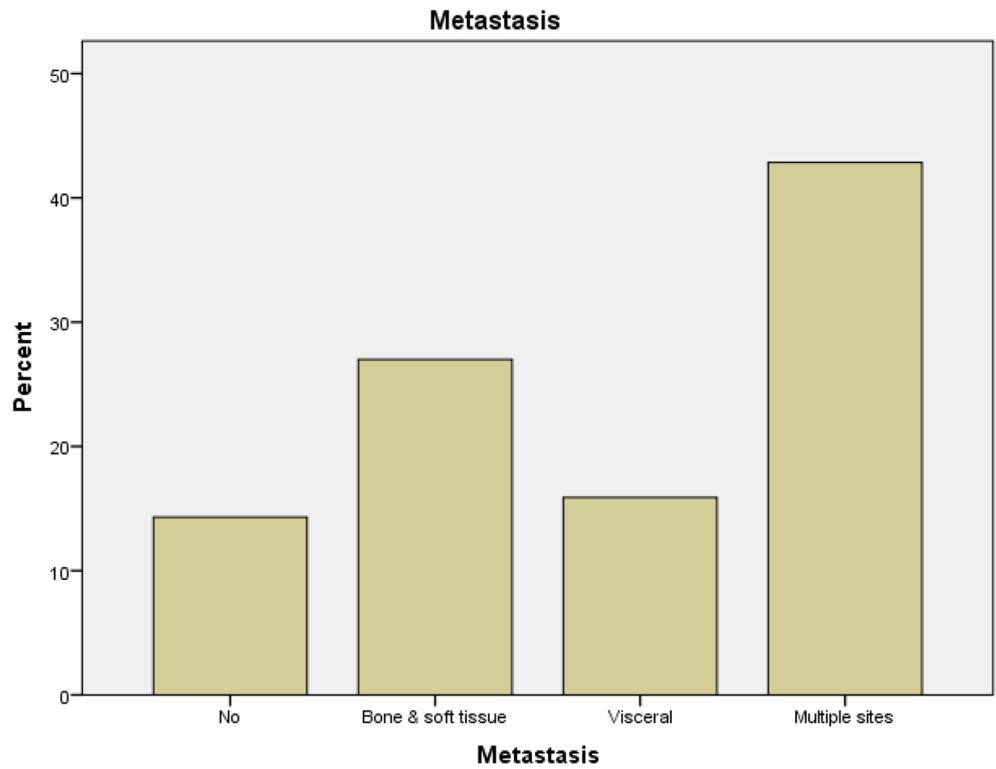
## Discussion

Although GnRh agonist/antagonist therapy has largely replaced the surgical ablation in practice, the problem of ovarian escape with failure to reach the postmenopausal levels was highlighted. In addition to this, the use of aromatase inhibitors in premenopausal women may be associated with activation of ovarian oestrogen secretion contradicting its value in breast cancer treatment [8].

The following are the sine qua non indications for surgical hormonal ablation in breast cancer patients: hormone receptor-positive breast cancer primary, recurrence and/or metastasis; premenopausal women, which are either menstruating regularly or having FSH  $\pm$  estradiol serum levels in the premenopausal range. In these cases, surgical ablation is usually done as a second- or third-line hormonal therapy after failure of previous lines (as proved by progression or recurrence), development of complication as thrombo-embolism, economical issues with the price of GnRH drugs or lack of patient compliance to the long-term therapy that extend for years.

For recurrent and metastatic luminal breast cancer patients, if chemotherapy did not induce menopause, probably ovarian suppression is needed until natural menopause. Thus, the potential reversibility of ovarian function with GnRH agonist/antagonist therapy is less likely to be an important issue for them [8].

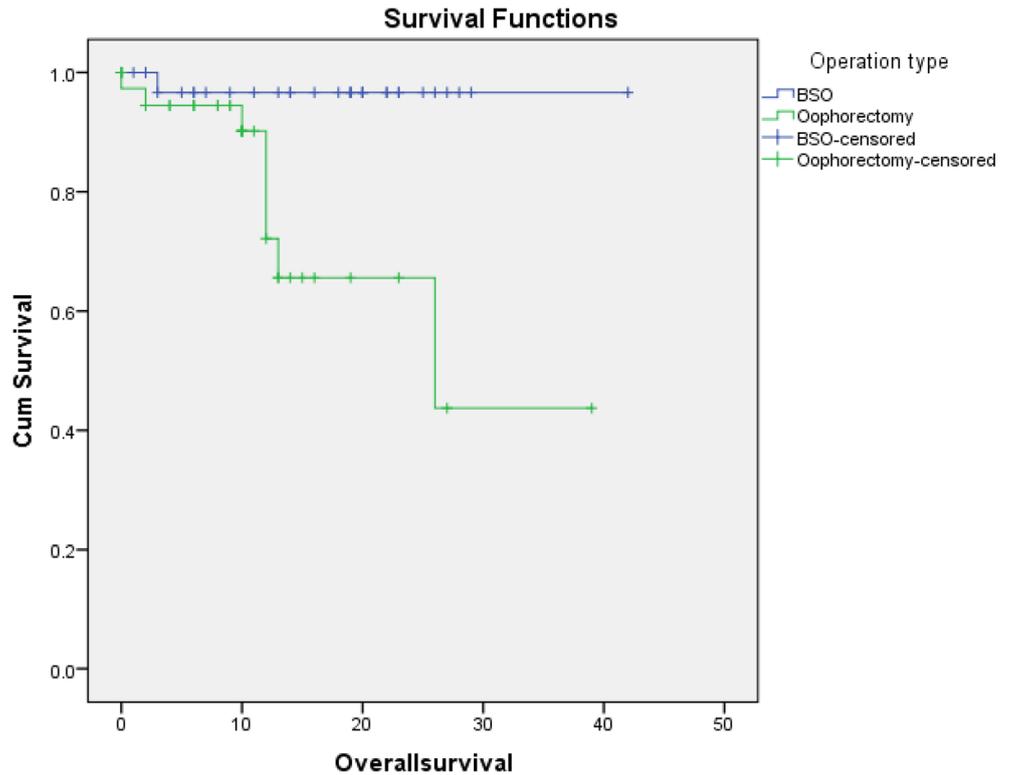
**Fig. 1** A bar chart showing different sites of metastasis in patients subjected to surgical hormonal ablation



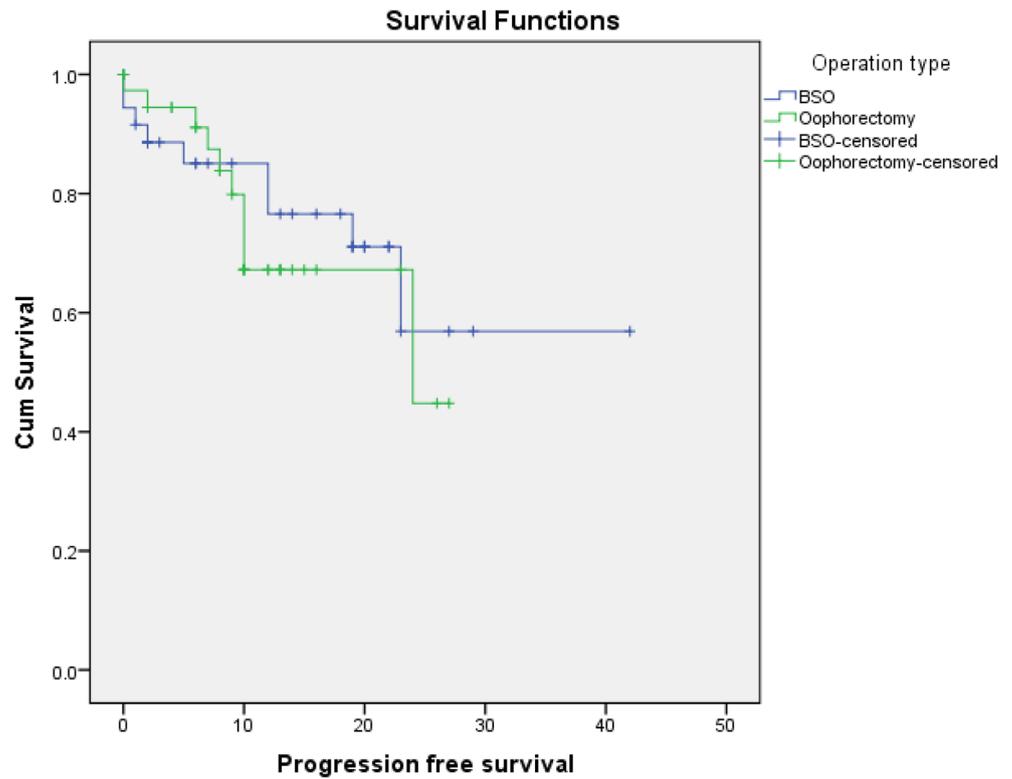
Bilateral salpingo-oophorectomy has long been described as a risk-reducing surgery for BRCA gene-mutated women by decreasing risk of both hormone-

positive breast cancer and gynecologic cancers (ovarian, fallopian and peritoneal) [9]. In this case, the fallopian tube is essentially removed as a part of the operation

**Fig. 2** Kaplan–Meier curve showing the estimated overall survival in patients who did bilateral salpingo-oophorectomy versus bilateral oophorectomy



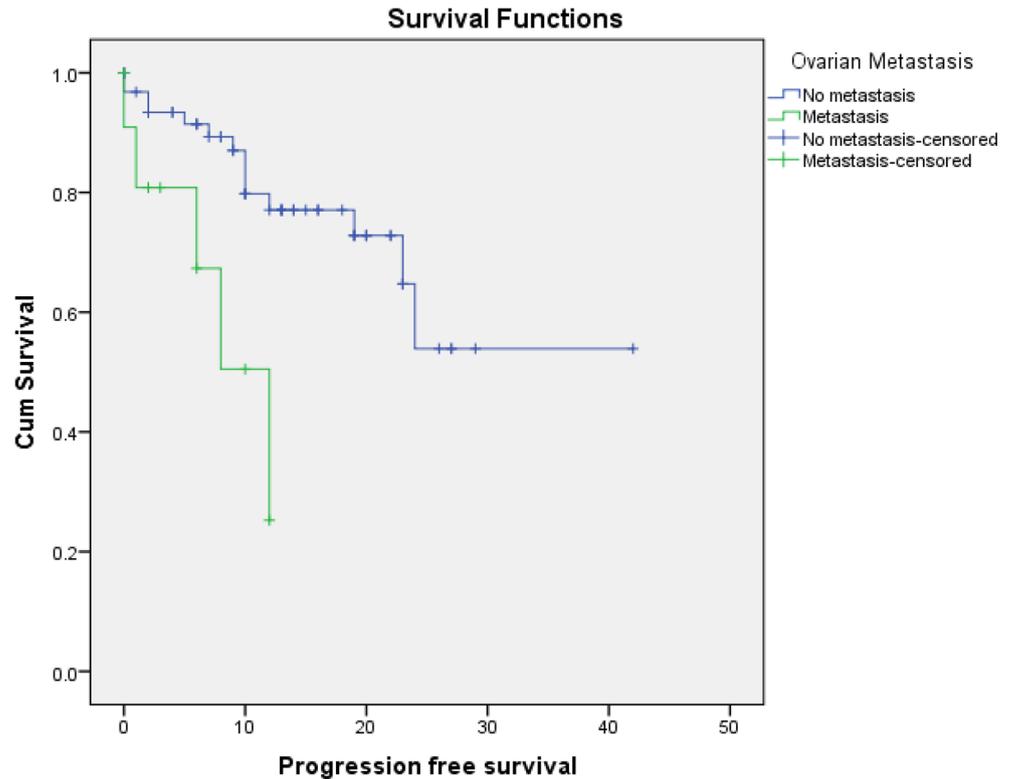
**Fig. 3** Kaplan–Meier curve showing the estimated progression-free survival in patients who did bilateral salpingo-oophorectomy versus bilateral oophorectomy



due to the recent theories suggesting that the epithelial ovarian cancer is actually arising from tube cells [10].

In our study, BRCA testing was not done for the patients. We compared the two techniques for surgical hormonal

**Fig. 4** Kaplan–Meier curve showing the estimated progression-free survival in patients with detected ovarian metastasis versus those with no detected malignancy in the ovaries



ablation practiced in our centre; BSO and BO (sparing the fallopian tubes) and the results showed a prolonged time lapse to progression (statistically insignificant) and prolonged overall survival ( $p$  value = .005) after the operation for the BSO group.

In our study, almost all patients underwent either procedures BO and BSO through multiport laparoscopy without need for conversion in any case and without recording complication (apart from wound infection necessitating debridement in one diabetic case and difficulty with extraction of specimen in another case necessitating wound extension). Thus, for the already established benefits of minimally invasive surgery of less pain, early ambulation and short hospital stay, plus the relative simplicity of the procedure, laparoscopy either single port or conventional is recommended whenever possible [11].

The incidence of occult ovarian metastasis in oophorectomy specimen done for hormonal treatment of breast cancer patients is not well studied. So, we identify it as about 15% and statistically clarify it as a prognostic sign of decreased overall survival ( $p$  value = .005) but not significantly affecting the progression-free period as noted before by Conte et al. [12].

Limitations of our study include being retrospective, relative small number of cases, patient compliance may have delayed the diagnosis of progression, and hormone testing was not done routinely on metastasis biopsies. Finally, randomized controlled trials are recommended.

## Conclusion

Surgical ovarian ablation is an effective line of endocrine therapy for luminal breast cancers with negligible morbidity. Laparoscopy should be the standard approach. Bilateral salpingo-oophorectomy is superior over simple oophorectomy for both progression-free and overall survival. An incidental finding of ovarian metastasis is a worse prognostic sign.

## Compliance with Ethical Standards

**Conflict of Interest** The authors declare that they have no conflict of interest.

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