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Resection of The Primary Tumor in Patients with Metastatic Breast Cancer, Impact on Patients' Survival, A Comparative Retrospective Study

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ABSTRACT

Background: Traditionally the treatment for women with metastatic breast cancer (MBC) is systemic therapy; surgery is for palliation or complications. Recently, challenges suggesting that primary tumor resection improve survival.

Aim of the work: This study was to evaluate surgical resection of primary breast tumor in female patients with MBC.

Patients and methods: The study included 230 females with MBC presented at Tanta University Hospital and Damanhour Medical National Institute throughout four years periods. They divided into two groups; Group (A); included 120 patients subjected to surgical resection to primary breast tumor and Group (B); included 110 patients subjected to non-surgical therapy for their primary breast tumor. We compared overall survival (OS), progression free survival (PFS) and other prognostic factors between both groups.

Results: The OS of surgical group was significantly longer than control group and PFS of those patients were better than controls but without significance. This outcome was more evident in patients with bone only metastases and/or with solitary or oligo-metastatic site(s).

Conclusion: In MBC radical surgery should have free margins. Wide local excision and mastectomy had equivocal results. Patients presented with bone only and/or solitary or oligo-metastatic site(s) have good outcome than controls and those with visceral and/or multiple metastatic sites.

Keywords: MBC, Metastatic breast cancer; OS, Overall Survival; PFS, Progressive Free Survival.

INTRODUCTION

Breast cancer (BC) is the most commonly occurring type of cancer in women worldwide. BC becomes more lethal and complicated during advanced and metastatic stages. According to the statistics, 20-30% of BC patients may obtain metastases soon after diagnosis and primary tumor treatment[1-3].

Of the total breast cancer cases, 20-30% end up having metastatic breast cancer (MBC), which eventually causes 400, 000 to 50,000 deaths annually across the world[4]. At the time of initial diagnosis, around 3.5% of women with breast cancer had already developed distant metastasis in the United States and this proportion is even higher in resource-poor settings[4,5].

According to the cancer statistics, around half of patients display clinically detectable metastatic disease when diagnosed. Furthermore, patients without metastasis at the time of diagnosis possess a high probability of having micro-metastasis sites that can't be detected using conventional detection techniques. Hence, metastasis is the most life-threatening consequence for patients diagnosed with cancer. Metastatic process comprises three distinct stages: invasion, intravasation, and extravasation [2,3,6].

Breast cancer patients' quality of life (QoL) is severely reduced with the cancer symptoms and side effects of the therapies. Indeed, physical and psychosocial functioning, family life, couple relations, and working ability affect the QoL in this population [3]. While there has been a growth in the literature to identify the needs of breast cancer survivors or affected cases with various stages, evidence-based, effective, and adaptable interventions for care are scarce [7,8].

It has been found in some studies that patient characteristics such as age and performance status are associated with the prognosis of patients with MBC. Moreover, it has been found in other studies that characteristics of tumors such as molecular type and histological grade are related to the survival of these patients. According to molecular type and other prognostic factors, specific treatment strategies, such as anti-HER2 therapy and endocrine therapy, could be adopted to improve the outcome of patients [9].

Systemic drug therapies such as chemotherapy, targeted drugs, hormone therapy, immunotherapy, and combinatorial therapies are the foremost treatment options for women diagnosed with stage IV breast cancer. Surgery and radiotherapy are also useful depending on the tumor stage and location. Hormone receptor positive (ER^+/PR^+) MBC is typically treated with hormone therapy (tamoxifen/aromatase inhibitor), and an amalgamation of hormone therapy with targeted drugs such as a cyclin-dependent kinase 4/6 (CDK4/6) inhibitor, everolimus, and phosphoinositide 3-kinase (PI3K) inhibitor is shown to improve the effectiveness of monotherapy. The combination of chemotherapeutics with anthracyclines or taxanes is an example of an effective treatment for metastatic BC [10,11].

Owing to advances in early detection and modern systemic therapy, the survival of patients with MBC improves over time and the risk of death decreases by 1% in each year. It is suggested that the

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improvement in survival is related to treatment as per the results from a large multi-center study [9].

Since metastatic breast cancer is considered an incurable disease with a worse prognosis, usually patients are provided with palliation and systematic therapy. Typically, breast surgery is performed if a woman presents with symptoms. Over the last many decades, it was believed that after metastasis, aggressive local treatment is not beneficial and therefore should not be considered as the treatment of choice. However, locoregional surgery by removing the breast and axillary tissues along with treating or doing surgery of meta-static site may reduce the symptoms and prevent cancer-related adverse outcomes [12-14].

AIM OF THE STUDY

The aim of this study was to find out the role of surgical resection of primary breast tumor in female patient with metastatic breast cancer.

PATIENTS AND METHODS

This study included 230 female patients presented with metastatic breast cancer; diagnosed and treated at Surgical Oncology Unit (General Surgery Department) and Clinical Oncology Department, Tanta University Hospital and Damanhour Medical National Institute throughout the period from September 2020 to January 2024.

Study design:

All patients included in this study had breast cancer associated with distant metastasis at the time of diagnosis. All patients had been treated with primary chemotherapy or hormonal therapy ± radiotherapy to metastatic disease, e.g., bone or brain. Data of patients were collected from the medical records of the included hospital. Patients were divided into two groups according to whether or not they underwent surgical resection of their primary tumor; Group (A) (the surgery group); included patients who were subjected to surgical resection to their primary breast tumor, (120 patients) and Group (B) (the control group); included patients who did not undergo surgical resection of their primary breast tumor at any time during follow-up (110 patients).

Inclusion criteria:

Age 18 year to ≤75 year, performance status: 0-1, with no previous therapy for breast cancer before presentation to our unit, with histopathological confirmation of breast cancer, having clinical or radiological evidence of distant metastasis, with adequate liver and kidney functions.

Exclusion criteria:

Patients with brain metastases were excluded from the study due to poor response to chemotherapy "as it doesn't cross the blood brain barrier"; and any patient who lost follow-up within six months and any patient who didn't continue the prescribed treatment.

Ethical considerations:

Before we start the research we toke the approval of the scientific committee of the Damanhour Medical Institute of Health University and an informed written consent was taken from each participant or their parents in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Study end points included death and recurrence of previously treated primary tumors or metastatic progression.

Definitions: Metastatic progression was defined as either a new site of metastatic disease or clinical or radiographic evidence of recurrence at a previously treated site or increasing tumor burden at a previously known metastatic site. Patients were categorized by site(s) of metastasis: bone-only, visceral only, bone and visceral.

Statistical analysis

Patient's characteristics were compared between surgery and control group. The collected data were tabulated and analyzed using SPSS version 16 software (SPSS Inc, Chicago, ILL Company). Categorical data were presented as number and percentages while quantitative data were expressed as mean±standard deviation (S.D), median, IQR and range. Chi-square test (X^2), or Fisher's exact test (FET) were used to analyze categorical variables. Coordinate of correlation was assessed by Cohen Kappa test was used to assess degree of agreement between 2 raters.

The overall survival (OS) and progression free survival (PFS) were reported for both surgery and control group and Kaplan-Meier curves were constructed. The log-rank test was used to compare the differences in survival and progression between the groups and P values < 0.05 were considered statistically significant.

Clinical Features: We reported history of changes "from medical records" of the breast size or asymmetry, nipple or areolar changes, skin changes, presence of breast lump and axillary swelling. Symptoms of metastases from breast cancer such as headache, blurring of vision or any symptoms of neurological deficit, bone pain or pathological fracture, yellowish discoloration of the sclera, localized or generalized abdominal distension, cough or dyspnea, weight loss or anorexia. General assessment data of the patients; data of local examination of the breast, regional lymph nodes, data of adequate systemic

examination for detection of metastases and TNM staging of the disease.

Investigations: Mammography and breast ultrasound data; to assess primary tumor, regional lymph node involvement, contra-lateral breast (in both groups) then post systemic therapy and/or radiotherapy that used to assess the tumor response during the periods of follow-up (in control group).

Cytological and histopathological examination data that included: FNAC, Tru-cut needle or open biopsy from the primary tumor to confirm the results of FNAC and to assess tumor type, grade, estrogen and progesterone hormonal receptor status (ER and PR) done to study Her2-neu over-expression. Data of metastatic work-up that included; chest X -ray and/or CT scan for detection of pulmonary metastases or pleural effusion, pelvi-abdominal ultrasound and/or CT scan to assess the presence of hepatic focal lesion(s), bone scan and/or MRI or CT scan and brain CT or MRI in selected cases.

Treatment:

Systemic therapy:

Systemic chemotherapy has been given to all patients of surgery group in the form of neoadjuvant and adjuvant chemotherapy. Primary chemotherapy has been given to 99 out of 110 (90%) patients of control group and hormonal only treatment has been given to the remaining eleven (10%) elderly, postmenopausal, frail patients with oligo-metastatic sites in whom the ER and PR receptors was strongly positive (Letrozole 2.5 mg once daily). Post chemotherapy hormonal treatment have been given to 42 out of 120 (35%) patients of surgery group with hormonal receptor positive in the form of anti-estrogen (Tamoxifen 10 mg twice daily) for 78 premenopausal patients (65%) and aromatase inhibitor (Letrozole 2.5 mg once daily) was given for 78 postmenopausal patients and to 99 out of 110 patients of control group (89.2%) with hormonal receptor positive in the form of tamoxifen for 11 premenopausal patients (10%) and letrozole for 62 postmenopausal patients (56.4%) with the same doses mentioned before (Table 1).

Table (1): Systemic therapy in surgery and control group

Systemic therapy	Surgery group (n=120)		Control group (n=110)	
	No	%	No	%
Chemotherapy only	42	35%	99	90%
Hormonal treatment only	0	0%	11	10%
Combined hormonal and chemotherapy	78	65%	62	56.4%

***Radiotherapy*:**

In the surgery group, primary breast field radiotherapy was given to 26 patients (21.7%) with wide local excision and tangential field radiotherapy was given to 52 out of 94 patients (55.3%) with modified radical mastectomy. Palliative radiotherapy (to metastatic site) was given for 28 patients (25.5%) with symptomatic and weight bearing bone metastases to the pelvis, vertebra and femurs in both surgery and control group.

Surgery:

Wide local excision and axillary dissection have been performed for 25 out of 120 patients (quadrantectomy for 18 patients and lumpectomy for seven patients). Modified radical mastectomy had been performed for 95 out of 120 patients in whom TRAM was performed for 6 patients (5%) who preferred immediate reconstruction. In all patients the resection margin was negative (Table 2).

Table (2): Surgical treatment variables

Type of surgery	No of patients	%
Wide local excision	25	20.8%
MRM mastectomy	95	79.2%
Resection margin:		
Negative	120	100%
Positive	-	0%

MRM Modified Radical Mastectomy

Follow up:

Follow-up of primary tumor site and regional lymph nodes:

Data of clinical follow-up for the patients of surgery group in the early postoperative period and regularly every 3 months were collected and used to detect and treat an early or late complication(s) related to surgery and to detect local tumor recurrence and for the patients of control group to detect and treat complication related to systemic therapy and/or radiotherapy.

Follow-up of metastases:

The metastases were followed-up by data of clinical examination and radiological imaging (Chest X-ray or CT scan, abdominal ultrasound or CT scan and bone scan) was done for patients to assess the response of metastases after surgery, systemic therapy and/or radiotherapy and to detect disease progression.

RESULTS

(I) ***Age incidence:***

In the present study the age of patients in surgery group ranged from 32-75 years with mean age of 50±13.16 years and median age of 47 years. Actually, using t-test to compare means of the 2 groups, the difference in age was highly significant, $P < 0.0001$ (Table 3).

Table (3): The age incidence among patients with metastatic breast cancer.

Age group in years	Surgery group (n=120)		Control group (n=110)		Total (n=230)	
	No	%	No	%	No	%
< 50 Years	60	50%	28	25.5%	88	38.3%
50-59 Years	24	20%	40	36.4%	64	27.8%
60-69 Years	20	16.7%	34	30.9%	54	23.5%
70-79 Years	16	13.3%	8	7.2%	24	10.4%

(II) Tumor characteristics:

***Primary tumor size and regional lymph node involvement*:**

The size of the primary tumor ranged from T_1 to T_4 in both study groups with highest incidence was T_2 (65.8% and 65.5%) in surgery and control group respectively while the regional lymph nodes involvement ranged from N_1 to N_3 in both study groups with highest involvement was N_1 (74.2% and 68.2%) in surgery and control group respectively (Table 4).

Table (4): Primary tumor size and regional lymph node involvement.

Tumor characteristics	Surgery group (n=120)		Control group (n=110)		Total (n=230)	
	No	%	No	%	No	%
Clinical T:						
T_1	15	12.5%	5	4.6%	4	8%
T_2	79	65.8%	71	65.5%	33	62%
T_3	6	5%	20	18.2%	7	13%
T_4	20	16.7%	14	12.7%	9	17%
Lymph node:						
N_1	89	74.2%	75	68.2%	164	71.3%
N_2	25	20.8%	25	22.7%	50	21.7%
N_3	6	5%	10	9.1%	16	7%

***Metastatic site(s)*:**

The bone was the commonest site of metastases in both study groups (50% and 43.6%) in surgery and control group respectively. The bone, liver, and lung were the least involved site in surgery groups (6.7%) and in control group (2.7%) (Table 5).

Table (5): Metastatic site(s)

Metastatic site(s)	Surgery group (n=120)		Control group (n=110)	
	No	%	No	%
Bone only	60	50%	48	43.6%
Bone and lung	15	12.5%	9	8.3%
Bone and liver	13	10.8%	13	11.8%
Bone, lung and liver	8	6.7%	3	2.7%
Liver only	24	20%	37	33.6%

***Number of metastatic sites*:**

The number of metastatic site(s) ranged from 1 to ≥3 sites in both study groups with the majority of patients had solitary metastatic site (70% and 77.3%) in surgery and control group respectively (Table 6).

Table (6): Number of metastatic sites in surgery and control groups.

Number of metastatic site(s)	Surgery group (n=120)		Control group (n=110)	
	No	%	No	%
1	84	70%	85	77.3%
2	28	23.3%	22	20%
≥3	8	6.7%	3	2.7%

(III) Histological subtypes, tumor grade and hormonal receptors status:

The most common histopathological finding in both surgery and control groups was invasive duct carcinoma, 90% and 91.8% respectively. In surgery group the tumor was moderately differentiated (GII) in 70%, while in control group; it was moderately differentiated (GII) in 83.6%. The estrogen and progesterone receptors were positive in 65.8% of patients in surgery group and 76.4% of patients in control group, while HER2-neu over-expression was positive in 30% of patients of surgery and 20.9% of patients of control group (Table 7).

Table (7): Tumor characteristics

Histological subtypes	Surgery group (n=120)		Control group (n=110)		Total (n=230)	
	No	%	No	%	No	%
IDC	**108**	**90%**	**101**	**91.8%**	**209**	**90.9%**
ILC	**12**	**10%**	**9**	**8.2%**	**21**	**9.1%**
Tumor grade:						
GII	84	70%	92	83.6%	176	76.5%
GIII	36	30%	18	16.4%	54	23.5%
ER-PR receptors:						
+Ve	79	65.8%	84	76.4%	163	70.9%
-Ve	41	34.2%	26	23.6%	67	29.1%
HER2-Neu:						
+Ve	36	30%	23	20.9%	59	25.7%
-Ve	84	70%	87	79.1%	171	74.3%

Results of follow-up:

The minimum follow-up period was 6 months, the maximum follow-up was 34 months and the mean follow-up was 16 months.

(I) Follow-up of primary tumor site and regional lymph nodes:

(A) Surgery group:

The patients of surgery group were followed in the early postoperative period and regularly every 3 months to detect and treat an early or late complication(s) related to surgery and to detect local tumor recurrence. In this group; wound seroma occurred in 6 (5%) patients, wound infection in 5 (4.2%) patients, an arm edema in 8 (6.7%) patients, paraesthesia in the axilla and medial chest wall in 6 (5%) patients and no tumor recurrence detected in any patient (Table 8).

Table (8): Local follow-up for surgery group

Complications	No of patients	%	Treatment and Outcome
Wound seroma	6	5%	Repeated aspiration and conservative treatment.
Wound infection	5	4.2%	Culture and sensitivity, daily dressing and broad-spectrum antibiotic.
Arm edema	8	6.7%	Conservative treatment
Paraesthesia at the axilla and medial chest wall	6	5%	Conservative treatment

(B) Control group:

The intact tumor and regional lymph nodes in control group were followed by clinical examination, ultrasound and mammography to assess their response to systemic therapy and/or radiotherapy (Table 9).

Table (9): Primary tumor and regional lymph nodes response in control group

Response	Primary tumor		Lymph nodes	
	No of patients	%	No of patients	%
CR	10/110	9.1%	34/110	30.9%
PR	66/110	60%	38/110	34.5%
SD	34/110	30.9%	38/110	34.5%
PD	0/28	0%	0/110	0%

CR = Complete response, PR = Partial response, SD = Stable disease, PD = Progressive disease.

(II) Follow-up of metastases:

(A) Surgery group

Patients with bone metastases: The metastases showed complete response in 6 out of 96 sites, partial response in 4 sites, stable disease in 5 sites and progressive course in two sites.

Patients with lung metastases: The metastases showed complete response in 19 out of 23 sites and partial response in 4 sites.

Patients with liver metastases*:* The metastases showed complete response in 4 out of 45 sites and partial response in one site. The other two patients died before follow-up.

(B) Control group

Patients with bone metastases: The metastases showed complete response in 11 out of 73 sites, partial response in 18 sites, stable disease in 29 sites and progressive course in 15 sites.

Patients with lung metastases: The metastases showed complete response in 4 out of 12 sites, stable disease in 6 sites and progressive course in 2 sites.

Patients with liver metastases: The metastases showed complete response in 13 out of 53 sites, partial response in 13 sites, stable disease in 16 sites and progressive course in 11 sites (Table 10, Photos 1-10).

Table (10): Follow-up and response of metastases in both surgery and control group

Metastatic site and response	Surgery group (n=120)		Control group (n=110)	
	No	%	No	%
***Bone*:**				
CR	37/96	38.5%	11/73	15.1%
SD	24/96	25%	29/73	39.7%
PR	31/96	32.3%	18/73	24.7%
PD	4/96	4.2%	15/73	20.5%
***Lung*:**				
CR	19/23	82.6%	4/12	33.3%
SD	0/23	0%	6/12	50%
PR	4/23	17.4%	0/12	0%
PD	0/23	0%	2/12	16.7%
***Liver*:**				
CR	25/45	55.6%	13/53	24.5%
SD	0/45	0.0%	16/53	30.2%
PR	20/45	44.4%	13/53	24.5%
PD	0/45	0.0%	11/53	20.8%

Photo 1: Preoperative bone scan shows left 5th rib mets (arrow).

Photo 2: Postoperative bone scan shows clearance of rib mets, which is found in photo 1.

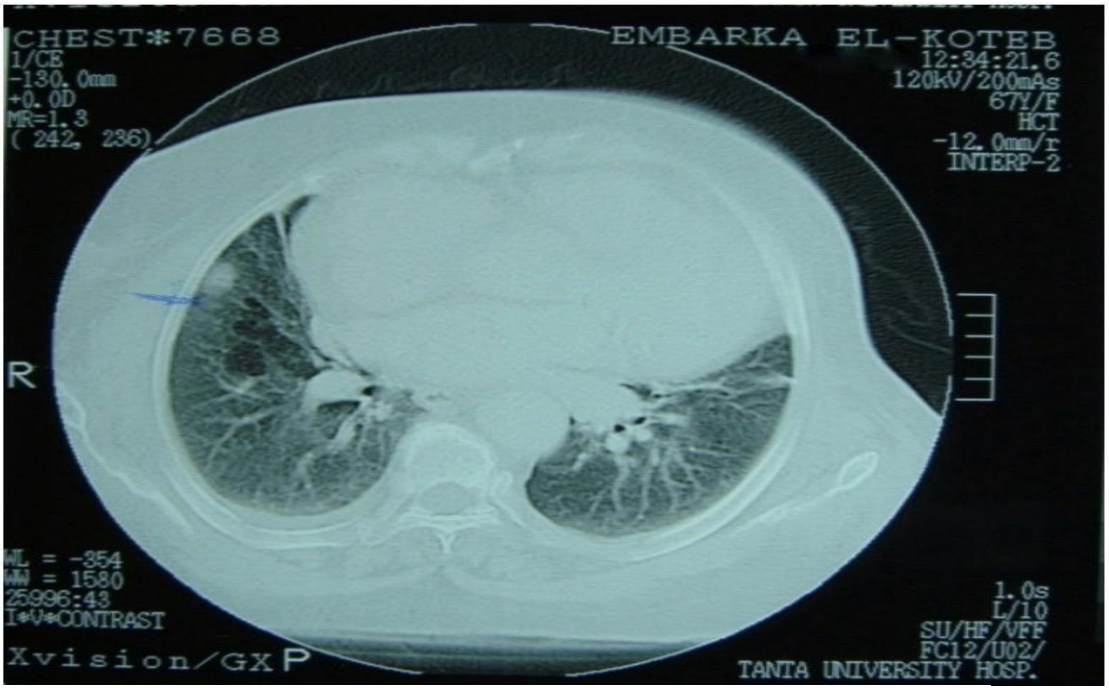


Photo 3: Preoperative CT chest shows right pulmonary solitary metastatic nodule (arrow)

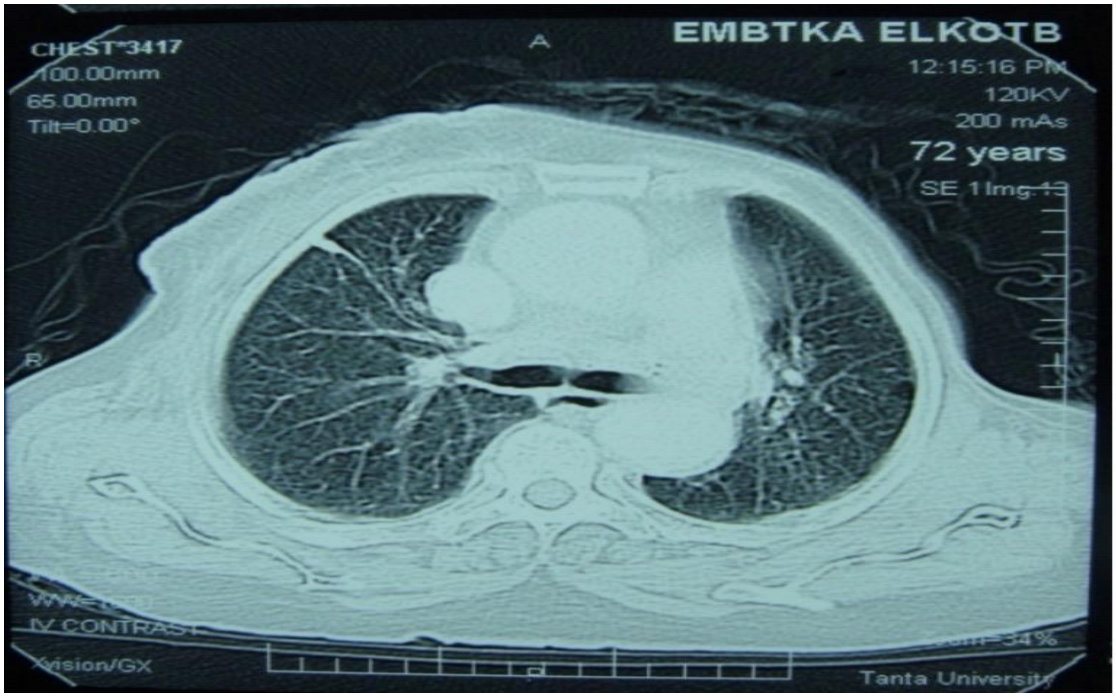


Photo 4 (Right): Postoperative CT chest shows disappearance of the nodule, which is found in photo 3.

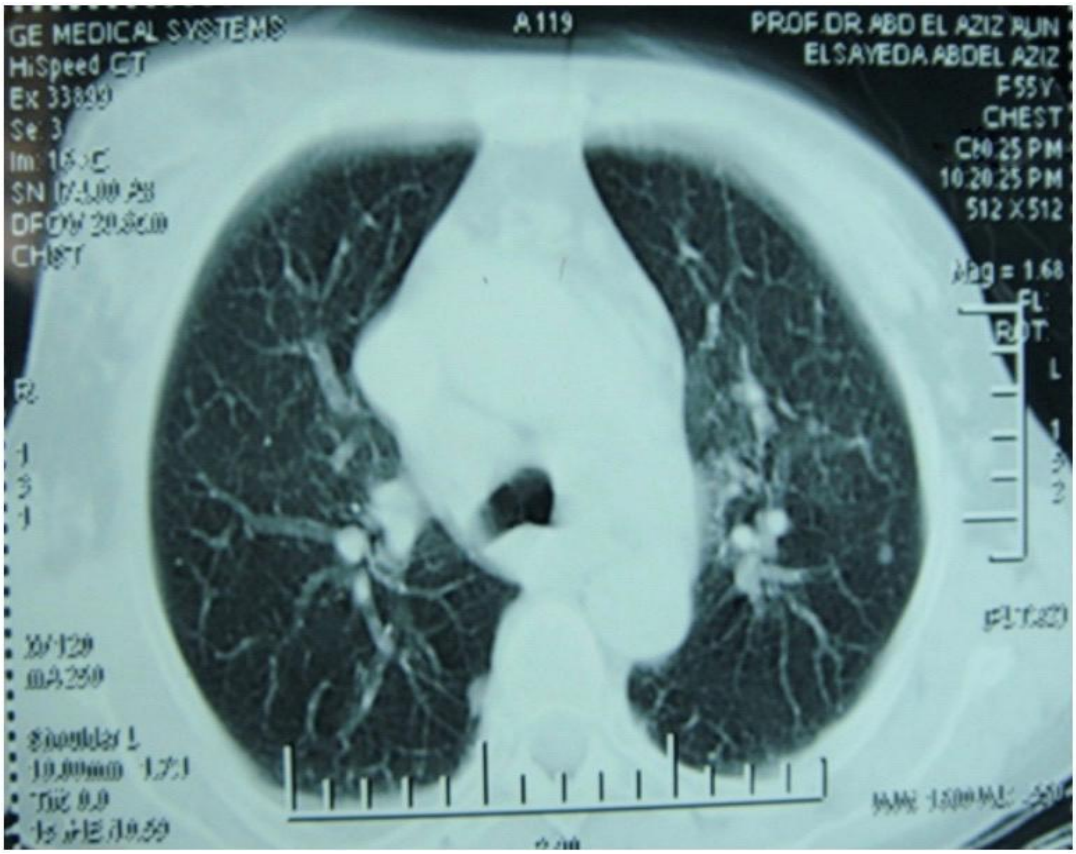


Photo 5: Preoperative CT chest shows bilateral hilar pulmonary metastases (arrows)

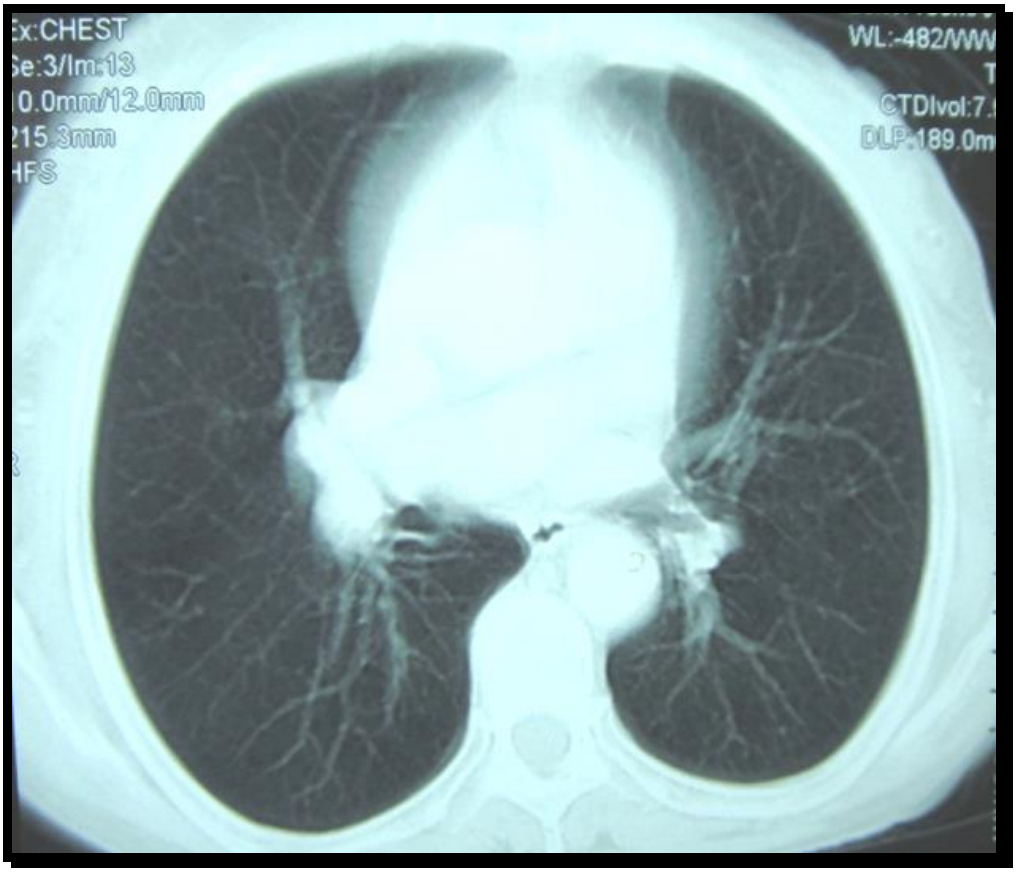


Photo 6: Postoperative CT chest shows disappearance of the metastases, which are found in photo 5.

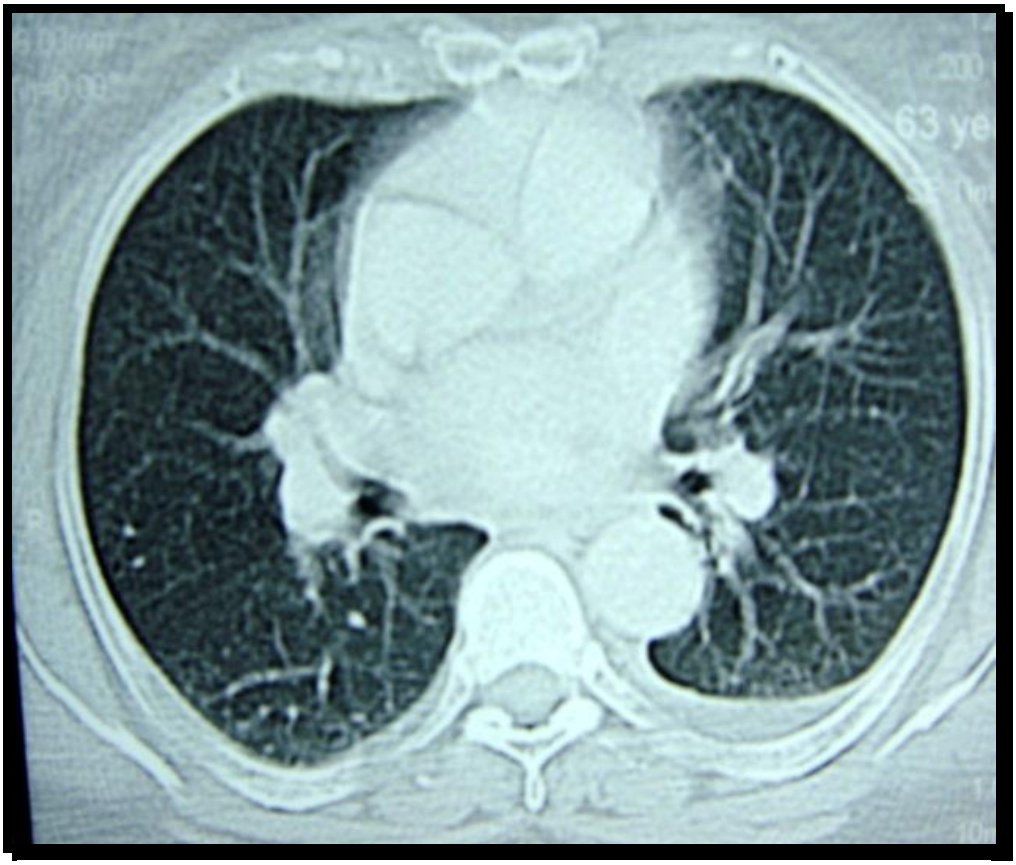


Photo 7: Preoperative CT chest shows left metastatic pleural effusion (arrow).

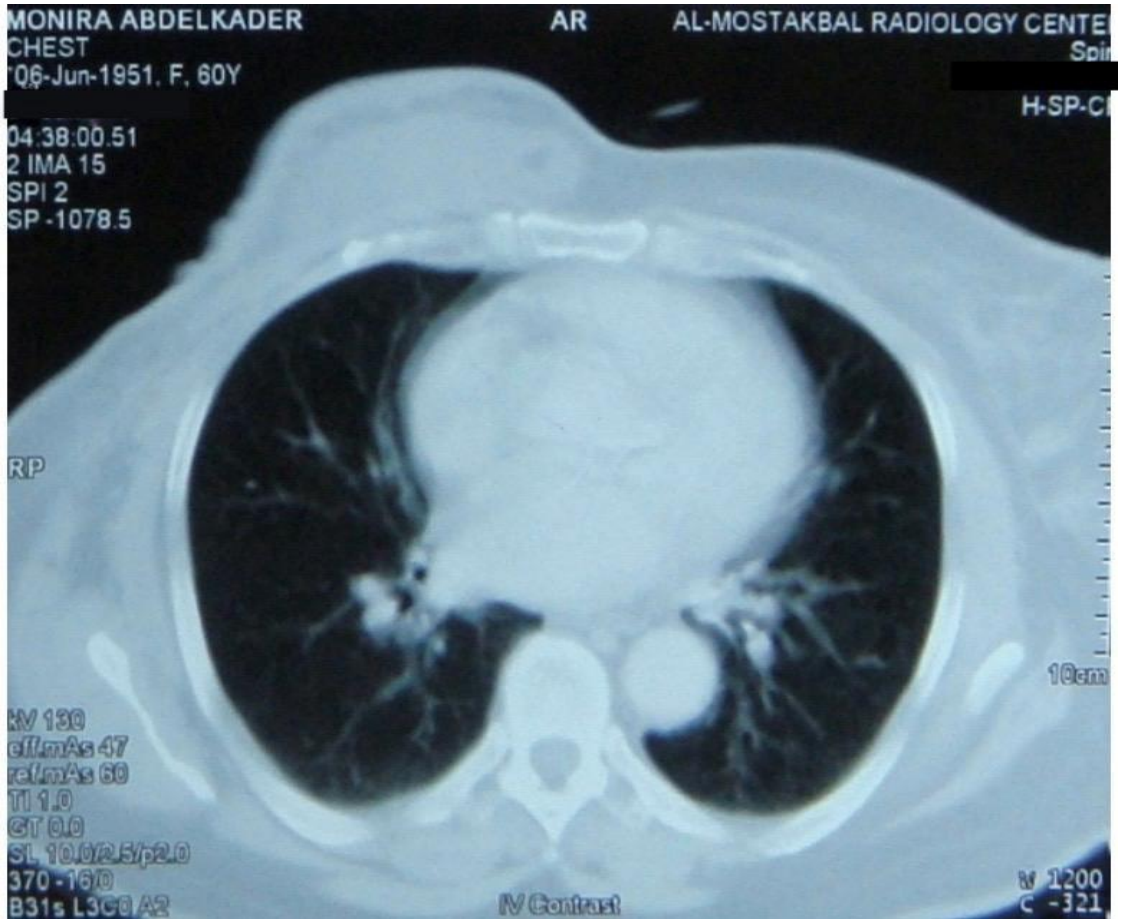


Photo 8: Postoperative CT chest shows clearance of the effusion, which is found in photo 7.

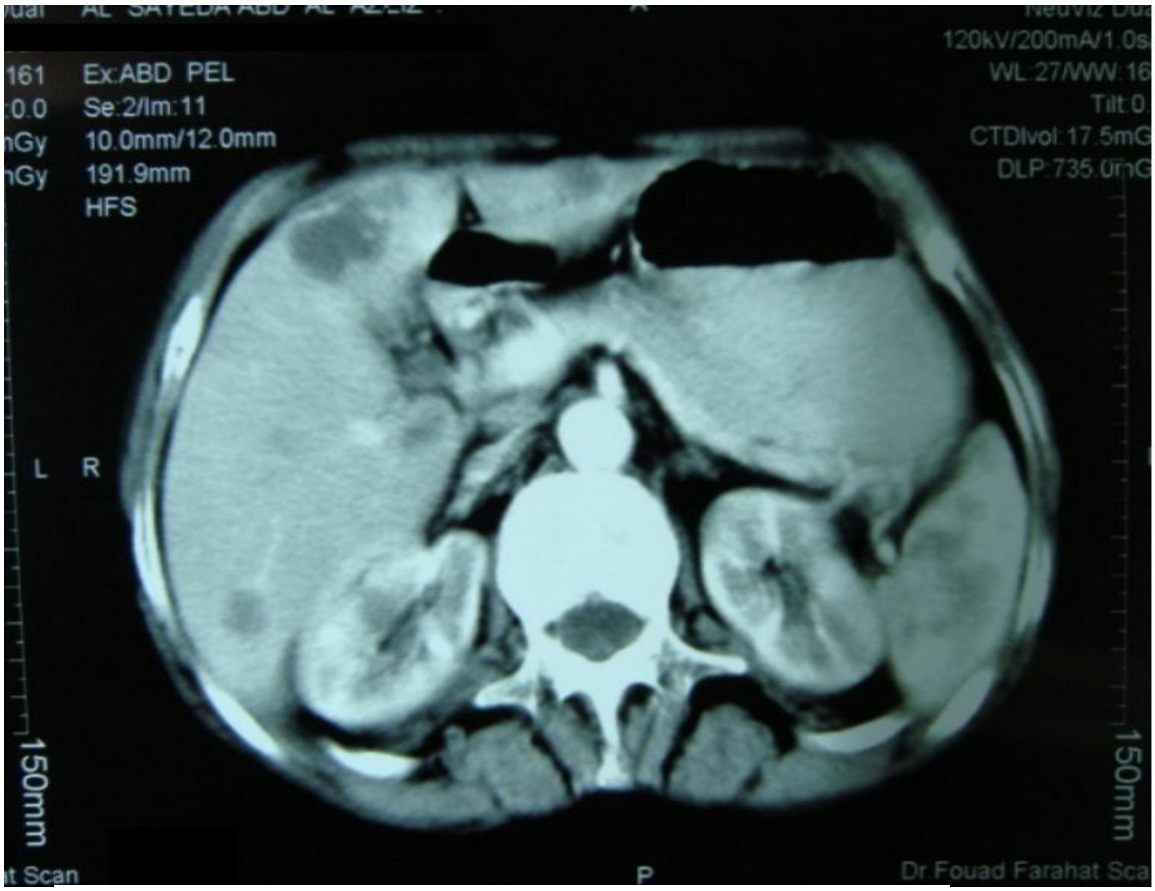


Photo 9: Preoperative CT abdomen shows multiple liver Mets (arrows).

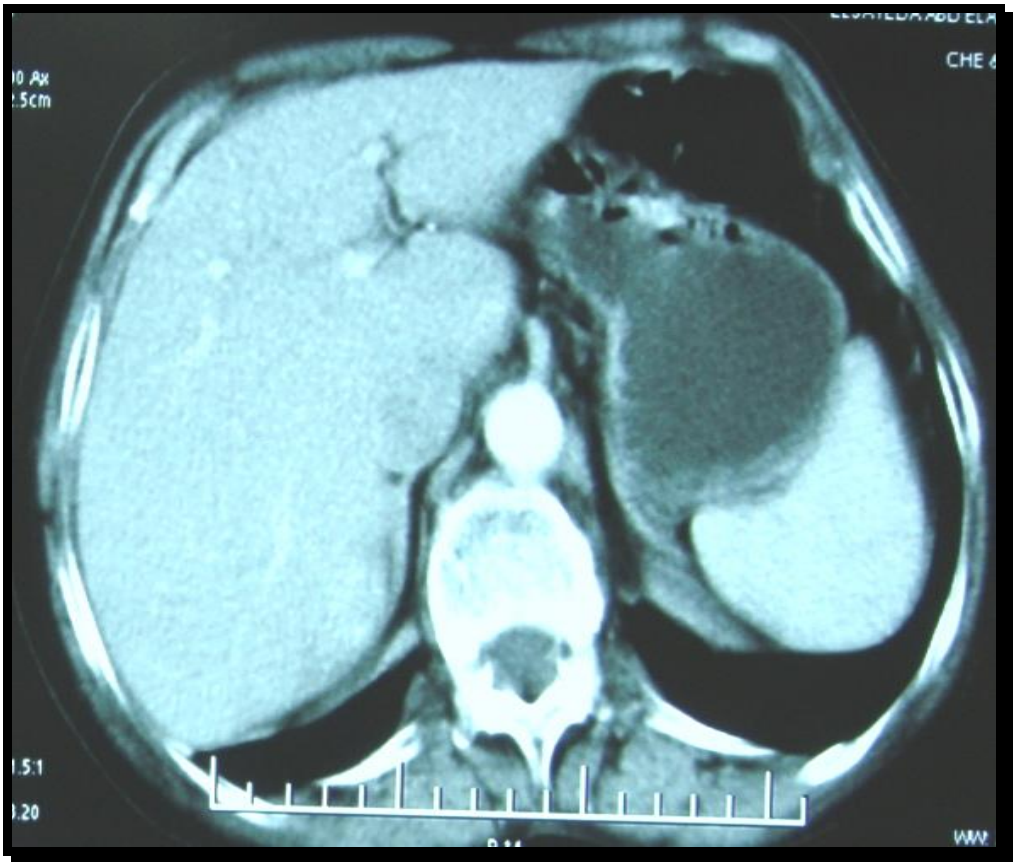


Photo 10: Postoperative CT abdomen shows clearance of all liver Mets, which are found in photo 9

Mortality:

In the present study there were 35 mortalities out of 230 patients (15.2%), 9 out of 120 patients in surgery group (7.5%) and 26 out of 110 patients in control group (23.6%). The nine patients of surgery group were old age, had multiple liver metastases, and associated comorbidity; 6 with bilharzial periportal fibrosis and mild liver cirrhosis, these patients developed liver cell failure, ascites and hepatic encephalopathy 6 months post-surgery. The other three had controlled atrial fibrillation and mitral valve replacement on oral anticoagulant, these patients developed uncontrolled arrhythmia and heart failure 3 months post-surgery.

The patients of control group were young age, ten of them had multiple liver metastases, seven of them developed secondary pulmonary metastases, malignant ascites and liver failure. Another three of had ischemic heart disease and developed acute myocardial infarction, also ten patients had multiple lung metastases; 6 of them had associated pleural effusions while four patients of them had associated bronchial asthma and developed respiratory failure, one developed secondary brain metastases and cerebrovascular stroke and the remaining three patients developed widespread skeletal metastases, pathological femoral fracture, deep vein thrombosis and pulmonary embolism (Table 11).

Table (11): Patients mortality in relation to type of metastases

Mortality	**Surgery group (n=120)**		**Control group (n=110)**	
	No	**%**	**No**	**%**
***Type of metastases*:**				
Liver	**6**	**66.7%**	**10/26**	**38.5%**
Atrial fibrillation	**3**	**33.3%**	**0/26**	**0.0%**
Lung	**0**	**0.0%**	**10/26**	**38.5%**
Bone and skeletal	**0**	**0.0%**	**3/26**	**11.5%**
Ischemic heart	**0**	**0.0%**	**3/26**	**11.5%**
***Factors affecting mortality*:**				
Age	**Yes**		**No**	
Co-morbidity	**Yes**		**Yes in one patient**	
Role of metastases	**No**		**Yes in 5 patients**	

Statistical analysis and survival:

The OS of patients in surgery group was longer than in control group (P = 0.002). The PFS for the patients subjected to surgery was better than control group (P = 0.531). The patients with bone only metastases subjected to surgical removal of their primary tumor had prolonged OS than patients not subjected to surgery (P = 0.009). Similar to the patients with combined bone and visceral metastases (P = 0.005) and patients with visceral only metastases (P = 0.082). The patients with single metastatic site subjected to surgery had prolonged OS than patients with multiple sites (≥ 2 sites) (P = 0.605). The patients of control group with solitary metastasis had longer OS than patients with multiple metastases (P < 0.001) (Fig. 1-3).

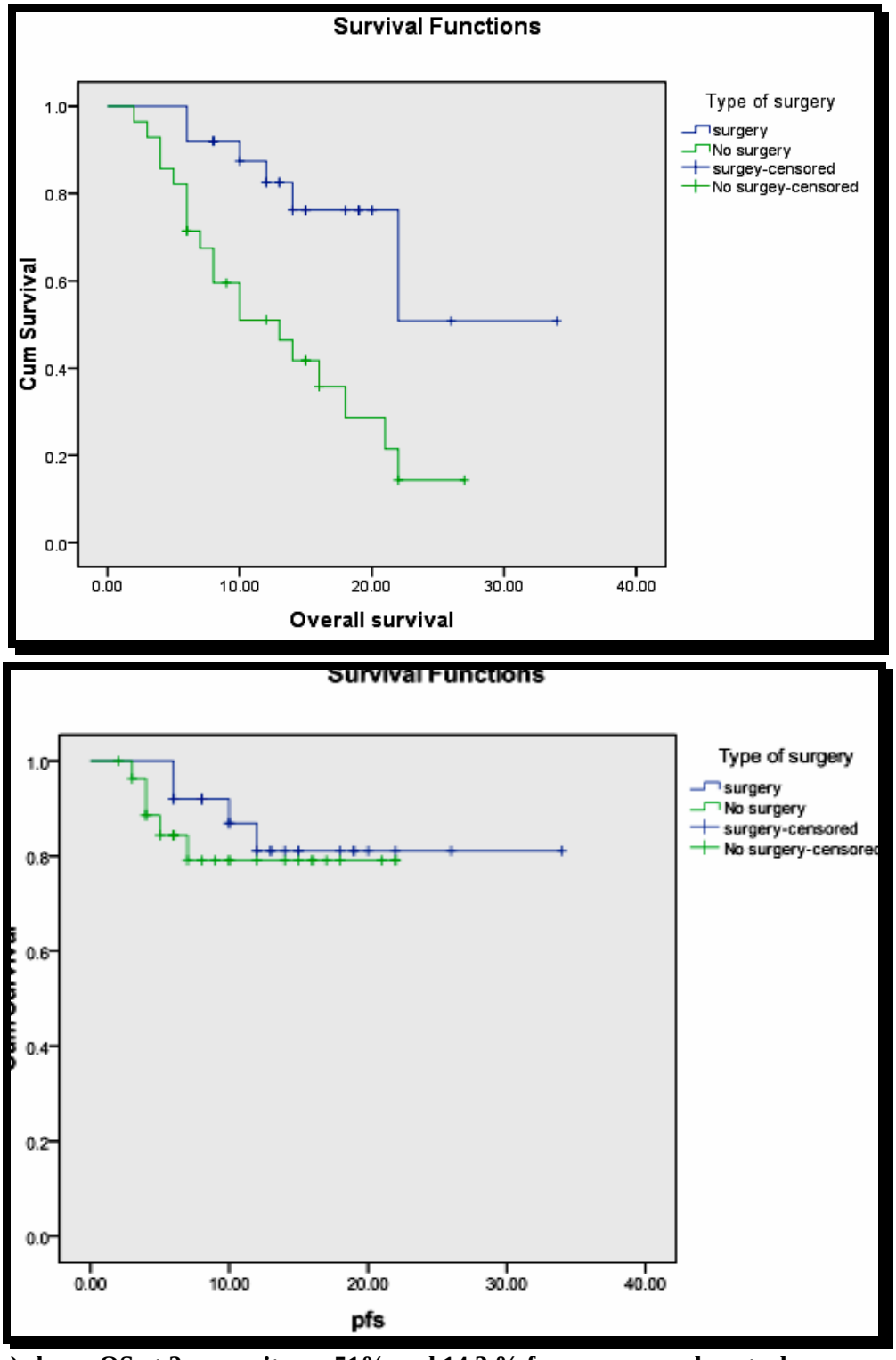
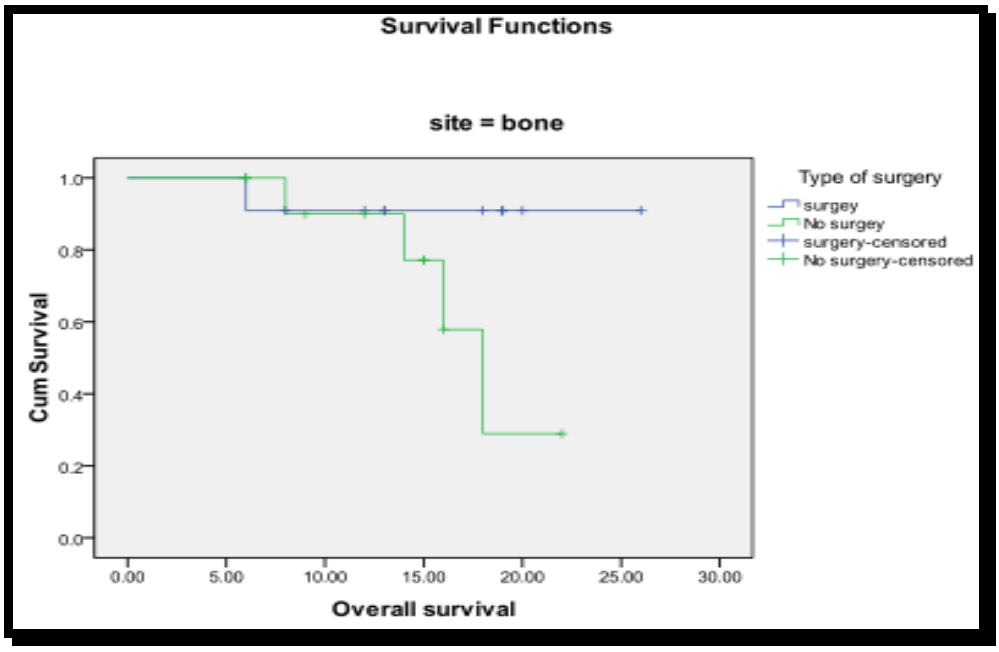
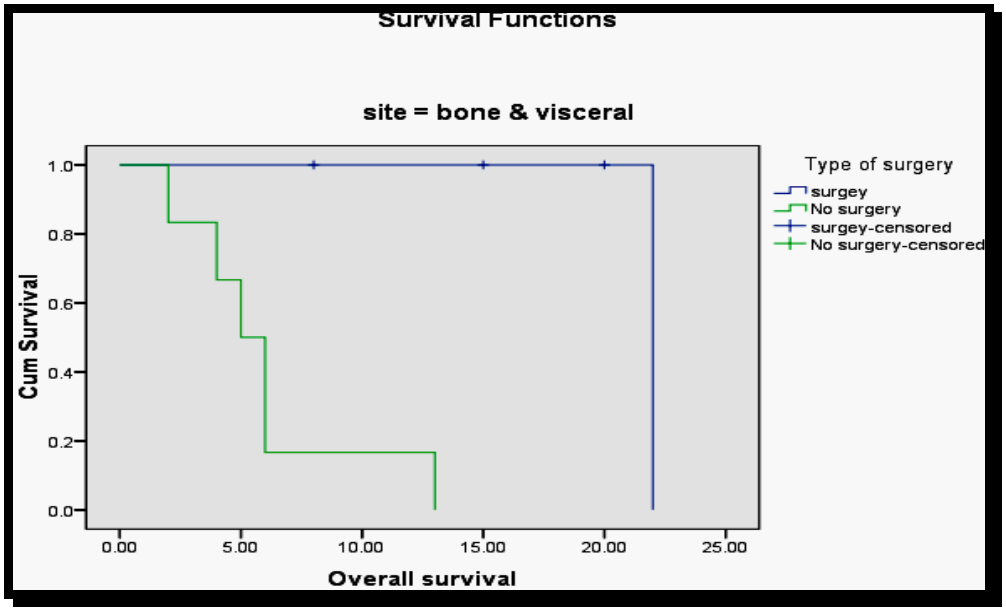


Fig (1): (Upper) shows OS at 2 years; it was 51% and 14.3 % for surgery and control group respectively (P=0.002). (Lower) shows PFS for surgery and control group.





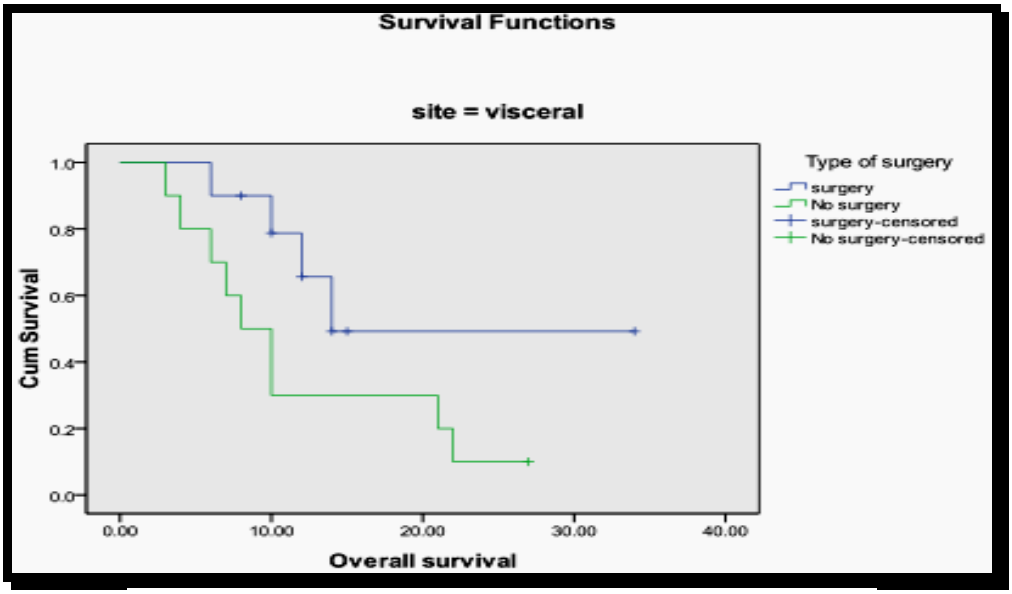


Fig (2): Shows OS at 2 years for different sites of metastases

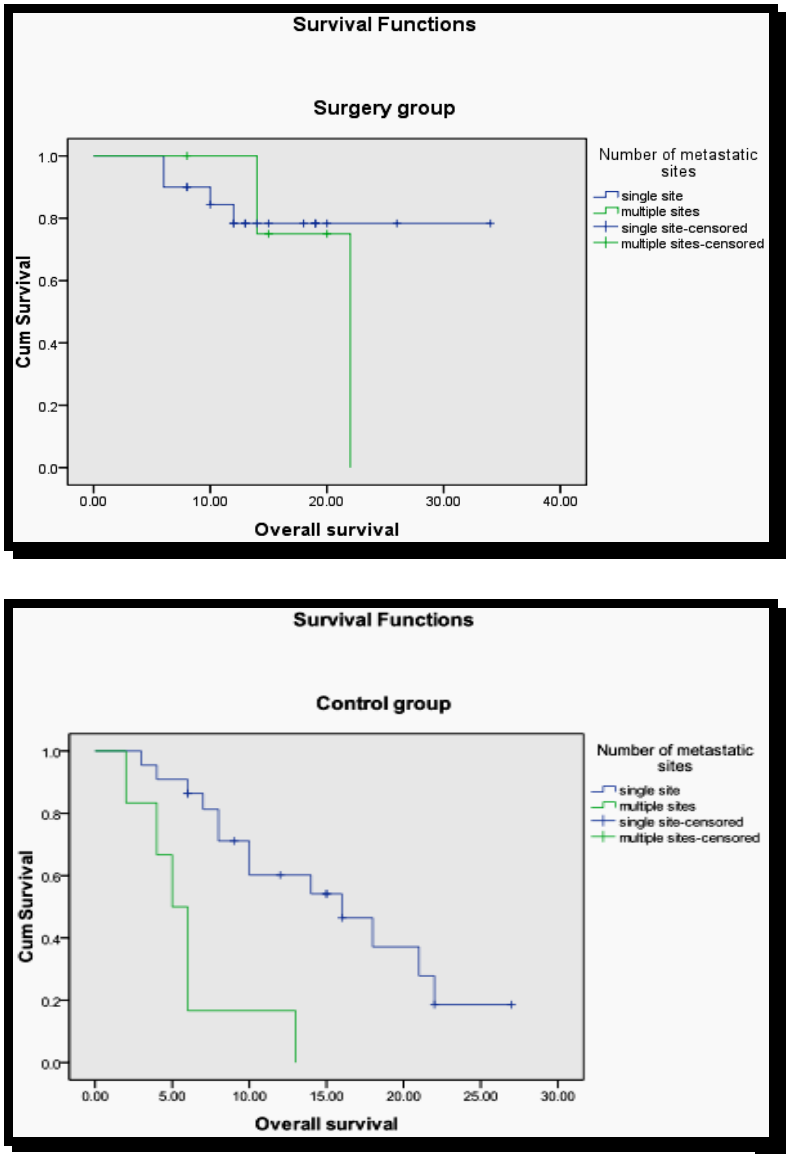


Fig (3): Shows OS at 2 years for surgery group in relation to number of metastases.

DISCUSSION

Unfortunately, in 20-30% of cases, cancer progresses to a metastatic stage. Metastatic breast cancer (MBC) is a chronic disease that requires longterm treatment to slow its progression. Although supportive care is a major asset in reducing the side effects (physical and psychological) of MBC and its treatments, the latter can considerably impact patient quality of life and can represent a barrier to the implementation of patients' personal and/or professional plans[(15)]. Over the last decade, the improvements in survival achieved with new therapies for metastatic breast cancer (MBC) have been groundbreaking.[16]

It has been reported that the 5-year survival rate for affected patients accounts approximately for 26% and patient's health can decline due to the metastasis lesions' invasion to vital organs, which can lead to formation of multiple foci that are hard to surgically remove and resistant development to the systemic therapies that are presently accessible.[17]

In the present study the patients subjected to surgery had longer OS than control group (P = 0.002).

Demirors and his colleagues, concluded in their study that locoregional therapy of the primary tumor and modern ST seem to be the perfect partners for better DFS and OS, which run in lines with our results.[18]

In the present study the progression-free survival for the patients subjected to surgery was better than control group. We performed wide local excision and axillary dissection for 25 out of 120 patients (20.8%) (quadrantectomy in 4 patients and lumpectomy in one patient). Modified radical mastectomy has been performed for 95 out of 120 patients (79.2%). In all patients the resection margin was negative. The survival was found to be equivalent for wide excision and mastectomy.

Olaogun and his colleagues, reported that a percentage of 20% of their patients were subjected to palliative simple mastectomy to reduce the tumor burden and the dose of systemic therapy, which

disagree with our results where we did modified radical in most of our cases (79.2%).[19]

In the present study the patients with single metastatic site subjected to surgery had prolonged OS than patients with multiple sites. Patients with bone only metastases had prolonged OS than patients with combined bone and visceral metastases or visceral only metastases.

Olaogun and his colleagues, concluded in their study that single metastasis had good outcome and survival rate than multiple metastasis and the same that bone metastasis has longer overall survival rate than soft tissue metastasis which run in lines with our results.[19] Also, **Ghali and his coworkers**, (2018), found in their study that single metastatic lesion has better overall survival rate than multiple metastatic lesions which agree with our results.[20]

Yang *et al.* found in their study that breast cancer with multiple metastasis with advanced lymph node invasion had poor overall survival than those with no incremented lymph node invasion, which run in lines with our results.[21]

Hu and his colleagues, documented in their study that ≤50 years old at primary diagnosis, DFS ≥24 months, adjuvant endocrine therapy, and absence of visceral, brain and multiple metastases were favorable prognostic factors.[9] In another study, **Bishop and his coworkers**, (2015), defied a complete response according to RECIST criteria as no-evidence-of disease (NED). They found attaining NED status was not related to OS, but it would influence the survival at 2 and 3 years.[22]

Wang and his colleagues, found in their study that patients with bone metastasis had the best survival, with 3-year OS rate of 50.5%, followed by patients with other metastasis, liver metastasis, and lung metastasis, (with OS rate of 41.9, 38.2, and 37.5% respectively) while patients with brain metastasis and multiple metastasis had worse OS than other subgroups: the 3-year OS rate was 19.9, and 27.4%, respectively), which agree with our results [(12)].

In the present study the patients of surgery group were subjected to surgery after neoadjuvant chemotherapy.

Olaogun and his colleagues, concluded in their study that patients subjected to surgery after having neoadjuvant systemic therapy had better prognosis and limitations of metastatic aggressiveness than those subjected to surgery directly and this was in agree with our results. The possible explanation is that those patients who underwent chemotherapy as their first line of treatment had a good response and were therefore believed to be candidates for potentially curative surgical intervention.[19]

CONCLUSION

Surgery was beneficial when performed after neoadjuvant chemotherapy. When resection of primary tumor in women with MBC is planned, it should be offered with a radical intent and free surgical margins should be obtained. The survival was found to be equivalent for wide local excision and mastectomy.

The patients subjected to surgical removal of the primary tumor, presenting with bone only and/or solitary or oligometastatic site(s) have an improved prognosis, longer OS and PFS than patients in control group, those with visceral and/or multiple metastatic sites. A well designed prospective multicenter studies are needed to reassess the paradigm ‘‘do not touch the primary tumor” in breast cancer patients with metastatic spread at diagnosis.

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